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BALANITIS XEROTICA OBLITERANS

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Balanitis xerotica obliterans (post-operationem) is the term which Stühmer [1] used in 1928 to describe an atrophic, shrinking process involving the glans and prepuce and frequently leading to urethral stenosis. On the basis of his first 5 cases Stühmer concluded that, although there was a close relation among various sclerosing processes of the male genitals described in the literature under the titles of leukoplakia and kraurosis, the condition in his cases was singular in that it developed in men in the second and third decades and followed circumcision for phimosis. In a second article he [2] described 4 more similar cases and expressed the opinion that balanitis xerotica obliterans was not identical with either kraurosis or leukoplakia of the male genitals.

Stühmer's euphonious title became a popular one; and several cases of sclerotic, atrophic dermatoses of the glans and prepuce have been reported before various foreign societies under the same name, and several contributions devoted to the subject have appeared, such as those by Müller,[3] Sprafke,[4] Grütz,[5] Beek [6] and de Gregario, de Blasio and

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1. Stühmer, A.: Balanitis xerotica obliterans (post-operationem) und ihre Beziehungen zur "Kraurosis glandis et praeputii penis," Arch. f. Dermat. u. Syph. **156**:613, 1928.

2. Stühmer, A.: Weitere Beiträge zur Kenntnis der Balanitis xerotica obliterans post-operationem, Arch. f. Dermat. u. Syph. **165**:343, 1932.

3. Müller, A.: Ein Fall von Balanitis xerotica obliterans, Dermat. Wchnschr. **93**:1372 (Aug. 29) 1931.

4. Sprafke, H.: Balanitis xerotica obliterans Stühmer, Dermat. Ztschr. **59**:27, 1930.

5. Grütz, O.: Beiträge zur Klinik der Balanitis xerotica obliterans, Dermat. Wchnschr. **105**:1206, 1937.

(Footnotes continued on next page)

Hijar.[7] No formal article devoted to the subject has appeared in the American literature, although balanitis xerotica obliterans was discussed by Madden [8] in his paper on the balanitides, and a case was recently presented at a meeting of the San Francisco and Los Angeles dermatologic societies by Novy.[9] For this reason we felt that a discussion of this relatively uncommon disease, and especially of its relation to leukoplakia, scleroderma, lichen sclerosus et atrophicus and kraurosis, was worth while. Considerable confusion exists especially among balanitis xerotica obliterans, kraurosis and leukoplakia of the male genitals.

Leukoplakia of the penis was first referred to in 1892 by Perrin,[10] who described a case in which the prepuce and frenulum were involved but the glans and urethra were normal. When the prepuce was retracted, its inner fold instead of being red was covered by a white, shiny coating which was rough in some places and smooth in others. The lesion of the prepuce formed a firm, apparently fibrous ring about the penis 1 inch (2.5 cm.) back of the coronal sulcus. Perrin and Leredde [11] described a second case in 1897, in which there were white sclerotic plaques on the glans and on the inner fold of the prepuce. Urethral stenosis was not noted. It was mentioned that some of the patches were rough and hypertrophic while others were smooth and atrophic.

Brandweiner [12] (1907), Kraus [13] (1907) and Fuchs [14] (1908) also reported white, patchy thickenings of the prepuce or glans under the title of leukoplakia. Fuchs even at that time compared the process to kraurosis vulvae. In these cases, however, no mention was made of atrophic retraction of the glans or of urethral stenosis.

In 1908 Delbanco [15] published 3 cases of what he termed kraurosis glandis et praeputii penis, characterized by a progressive, atrophic retrac-

6. Beek, C. H.: Ueber die Kraurosis glandis et praeputii und die Balanitis xerotica obliterans und über ihre Beziehungen zueinander, Acta dermat.-venereol. **19**:603 (Dec.) 1938.

7. de Gregario, E.; de Blasio, R., and Hijar, A.: Balanitis inflammatoria chronica atrophicans et sclerosans, Ann. de dermat. et syph. **10**:588 (July) 1939.

8. Madden, J.: The Balanitides, J. A. M. A. **105**:420 (Aug. 10) 1935.

9. Novy, F. G., Jr.: Balanitis Xerotica Obliterans, Arch. Dermat. & Syph. **43**:397 (Feb.) 1941.

10. Perrin, L.: Posthite chronique d'aspect leucoplasique, Ann. de dermat. et syph. **3**:22, 1892.

11. Perrin, L., and Leredde: Balano-posthite chronique leukoplasique, Ann. de dermat. et syph. **8**:1286, 1897.

12. Brandweiner: Leukoplakie der Glans penis und des inneren Praeputialblattes, Arch. f. Dermat. u. Syph. **86**:137, 1907.

13. Kraus, A.: Ueber Leukoplakia (Leukokeratosis) penis, Arch. f. Dermat. u. Syph. **86**:137, 1907.

14. Fuchs, B.: Zur Kenntnis der Leukoplakia penis, Arch. f. Dermat. u. Syph. **91**:91, 1908.

15. Delbanco: Kraurosis glandis et praeputii penis, Arch. f. Dermat. u. Syph. **91**:384, 1908.

tion of the glans and inner fold of the prepuce leading to stenosis of the urethral meatus. The disease was accompanied by intense itching and disagreeable paresthesias. Delbanco stated the belief that kraurosis was a disease sui generis differing from the condition in cases of leukoplakia described by Kraus and Fuchs.

In 1910 Galewsky [16] discussed 6 cases of "leukokeratosis" (kraurosis) of the glans and prepuce, alining them with those of Delbanco. Galewsky emphasized the difficulty of distinguishing kraurosis from leukoplakia when the location was on the penis.

In 1925 Benedek,[17] from a study of 3 cases and a thorough survey of the literature, concluded that there was a disease consisting of leukokeratotic lesions of the genitals characterized by pure hyperplasia and hypertrophy, to which he applied the term leukokeratosis. In contrast was the condition in cases such as those of Delbanco and Galewsky, presenting the histologic picture of atrophy, for which he reserved the term kraurosis. He suggested the name leukosclerokeratosis for the condition in which leukoplakic (hypertrophic) as well as kraurotic (atrophic) changes were present simultaneously. He expressed the opinion that leukokeratosis, leukosclerokeratosis, kraurosis and even subsequent malignant degeneration were closely related and represented various stages of the same pathologic processes.

Genner and Nielsen,[18] in 1931, published an extensive article dealing with leukokeratosis and kraurosis of the penis and described 3 cases under the title leukokeratosis. The authors concluded that on the basis of all available experience the exact relation of leukokeratosis (leukoplakia) and kraurosis to one another was not clearly established. For a more detailed consideration of the pertinent literature reference may be made to the publications of Benedek or Genner and Nielsen.

CLINICAL FEATURES

We have studied a total of 18 cases of balanitis xerotica obliterans, and Dr. Harry Foerster sent us histologic sections from an additional case (Michelson, 9 cases; Sweitzer, 3; Madden, 3; Freeman, 1, and Laymon, 2). The disease occurred at various ages, ranging from 22 to 65. A relation to circumcision could not be determined in any of the patients, and a history of repeated attacks of balanoposthitis was notably absent except in 1. Each of the patients presented much the same picture, which will be described in detail in another part of the paper. Urethral stenosis was present in all.

16. Galewsky: Ueber Leukokeratosis (Kraurosis) glandis et praeputii, Arch. f. Dermat. u. Syph. **100**:262, 1910.

17. Benedek, T.: Leukokeratosis glandis penis verrucosa et simplex, Dermat. Wchnschr. **81**:1135, 1925.

18. Genner, V., and Nielsen, J.: Leukokeratosis and Kraurosis of Penis, Acta dermat.-venereol. **12**:195, 1931.

Stühmer characterized balanitis xerotica obliterans as an obliterative, cicatricial, sclerotic, shrinking process involving the perpuce and glans. In his patients, who were relatively young (under 40), the lesions appeared as a rule several months after circumcision or dorsal incision of the prepuce for phimosis. The disease, however, is not exclusively limited to young persons, as illustrated by such patients as those of Morimoto [19] (64 years old), Müller (66 years old) and Grütz (4 patients over 50) and several of ours. Also, since Stühmer's article was published, identical conditions have been described in patients who had never had a circumcision or dorsal incision; hence it must be assumed that an operative procedure is not a requisite for the diagnosis of balanitis xerotica obliterans. For example, in 5 of the 12 cases described by de Gregario, de Blasio and Hijar there had been no previous operation of any kind.

The early symptoms of the disease vary in acuity and intensity. They may be of insufficient severity to force the patients to seek medical advice, so that when the patient is first seen by a physician the disease is in full development. The early changes are especially apt to remain unnoticed if the prepuce is long, and they may consist of only a few erythematous areas on the prepuce or glans. We have observed patients, however, in whom the disease appeared abruptly and in its early phases underwent an extremely stormy course. There was intense pain, itching, burning and prickling with profuse purulent secretion and in one instance sloughing of the distal half-centimeter of the urethra so that it hung from the meatus and had to be clipped away. Later in the course of the disease there may be pain on erection, diminution in sensation on the glans and disturbance of the sexual function.

Balanitis xerotica obliterans is chronic and, as a rule, slowly progressive. From the observation of our own cases, however, it should be stated that the disease in certain cases may run a somewhat cyclic course characterized by periods of decided improvement, the skin apparently becoming less sclerotic and the urethral stenosis less intense. In his patients who had been circumcised Stühmer referred to balanitis xerotica obliterans as a pterygium-like growth appearing at the point of excision of the prepuce and extending onto the glans. In patients who have not been circumcised there is an almost constant involvement of the prepuce in the form of a constricting, sclerotic band which is located 1 or 2 cm. from the distal end. As the disease progresses, the coronal sulcus may partially or completely disappear, and the frenulum may be obliterated or sclerosed. There may be adhesions between the prepuce and the glans.

19. Morimoto, S.: Ein Fall von Balanitis xerotica obliterans, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **43**:234, 1932.

The involvement of the glans may or may not be diffuse. If it is, the glans is white, bluish white or ivory colored. If it is not diffuse, the admixture of white plaques and the normal red tissue of the glans gives rise to a mottled appearance. In Novy's case there were areas of telangiectasia resembling roentgen ray dermatitis. The glans may appear shriveled, although when stretched between the fingers the skin is thin, smooth and shiny. Müller mentioned the resemblance of the lesions to parchment. The affected tissues are more friable than normal, so that tiny fissures appear, especially on the prepuce and on the frenulum. Erosions and hemorrhagic or serous subepidermal bullae, especially near the meatus, may accompany the cicatricial changes. We noted hemorrhagic bullae in one of our cases early in the course of the

Fig. 1.—Balanitis xerotica obliterans in a man aged 33. The disease began insidiously in 1938. *A*, note the constriction of the prepuce and the atrophic white plaques on the glans. *B*, there is considerable stenosis of the meatus and extensive involvement of the glans.

disease. Carcinoma may be an eventual development, as exemplified in cases described by Stühmer, Frühwald [20] and Grütz.[5]

Another noteworthy and constant feature of balanitis xerotica obliterans is the gradual narrowing of the urethral meatus, often leading to complete stenosis, which renders urination increasingly difficult and finally impossible. Gayet [21] stressed the potential dangers of a meatal stricture, stating that it may lead to urinary retention, damage to the posterior urethra, bladders and kidneys or even perineal phlegmon.

20. Frühwald: Peniscarcinom nach Balanitis xerotica obliterans (Stühmer), Zentralbl. f. Haut- u. Geschlechtskr. **50**:98, 1935.

21. Gayet, G.: A propos de la "balanitis xerotica obliterans," Lyon méd. **161**:25 (Jan. 9) 1938.

HISTOLOGIC FEATURES

De Gregario, de Blasio and Hijar pointed out that histologic studies lead one to believe that balanitis xerotica obliterans is related pathogenetically to a series of recurring subacute or chronic inflammatory processes in which restitutio ad integrum is impossible and which eventually lead to a state of cicatrization or sclerosis.

Early in the course of the disease inflammatory changes predominate. The epithelium is invaded by polymorphonuclear leukocytes, and at first there is an abundant, diffuse, cellular infiltrate in the papillary portion of the edematous cutis with large numbers of the same type of cells. Later, the relative number of lymphocytes increases, and epithelioid and plasma cells may be present. In the subacute phases the lymphocytic infiltrate becomes arranged about the vessels.

During the evolution of the process histiocytes proliferate intensively in areas which later are centers of cicatrization. De Gregario, de Blasio and Hijar noted that migratory cells tended to disappear as the connective tissue became denser and that the walls of the blood vessels became reduced to a single layer of endothelium. Proliferation of connective tissue seemed most accentuated about these vessels.

In the fully developed condition there is distinct atrophy of the epidermis, but with relative and absolute hyperkeratosis. There may be a moderate degree of intracellular edema in the lower portions of the epidermis and slight liquefaction degeneration of the basal cell layer. A sprinkling of lymphocytes may be noted directly beneath the basal layer. Perhaps the most striking histologic feature of balanitis xerotica obliterans is the band of homogenization in the upper portion of the cutis. This area appears relatively acellular and edematous and may show diminution or complete disappearance of the elastic tissue. To this point the histologic pictures of balanitis xerotica obliterans and lichen sclerosus et atrophicus are practically identical. However, in balanitis xerotica obliterans we have not observed a bandlike formation of the infiltrate as is frequently seen in lichen sclerosus et atrophicus just below the homogenized zone. In the middle and deeper portions of the cutis there is a lymphocytic perivascular infiltrate.

RELATION TO AND DIFFERENTIATION FROM OTHER DISEASES

One of the most difficult aspects in the diagnosis of balanitis xerotica obliterans is its relation to and differentiation from similar and probably closely related processes involving the male genitals, including the following diseases: (*a*) erythroplasia of Queyrat, (*b*) circumscribed scleroderma, (*c*) lichen sclerosus et atrophicus, (*d*) lichen planus, (*e*) kraurosis and (*f*) leukoplakia.

A. Erythroplasia of Queyrat.—Sulzberger and Satenstein [22] first recorded this condition in America as a rare form of precancerosis. The lesions, which may occur on the glans or prepuce, are well defined, slightly elevated patches with brilliant red, velvety surfaces. Thus the efflorescences are entirely different from the thin, white, sclerotic plaques of balanitis xerotica obliterans. Histologically there is hypertrophy rather than atrophy of the epidermis. Peyri,[23] however, classified erythroplasia

Fig. 2.—Photomicrograph showing especially the atrophy of the epidermis and the homogenization of the upper part of the cutis.

as a type of kraurosis, dividing the latter into an atrophodermic (Delbanco) type, a white or leukoplakic type and a red or erythroplasic type. It seems to us that neither clinical nor histologic differentiation between erythroplasia and balanitis xerotica obliterans should present serious difficulty.

22. Sulzberger, M. B., and Satenstein, D. L.: Erythroplasia of Queyrat, Arch. Dermat. & Syph. **28**:798 (Dec.) 1933.

23. Peyri, J.: Die reine weisse and rote Kraurosis der Gegend von Eichel und Praeputium, abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **23**:383, 1927.

B. Circumscribed Scleroderma.—Scleroderma occurs extremely rarely on the male genitals. Pautrier and Camus,[24] in 1932, reported the case of a patient who presented a ring of scleroderma about the glans and prepuce. In 1934 Gougerot, Degos and Roulle [25] described 2 similar cases and stressed the difficulty in making such a diagnosis if there were no lesions elsewhere on the body. In 1939 Gougerot and Basset [26] reported the case of a boy aged 19 in whom two sclerotic rings developed on the glans and prepuce three weeks after an attack of balanitis. In this case the urethral meatus was contracted and infiltrated. In the discussion of the case Clement Simon proposed a diagnosis of balanitis xerotica obliterans. Touraine also related an interesting case which he had studied in which there was typical balanitis xerotica obliterans with scleroderma *en bande* of the abdomen and inguinal regions. For this reason he felt that balanitis xerotica obliterans was a part of scleroderma. In his discussion of balanitis xerotica obliterans Madden expressed his belief that the disease was closely related to morphea. In our opinion, however, the histologic picture affords a means of differentiating scleroderma from balanitis xerotica obliterans. In the former there is an actual increase in number and thickening of the individual connective tissue fibers throughout the whole cutis, as contrasted with the edematous, homogenized zone in the upper part of the cutis in balanitis xerotica obliterans.

C. Lichen Sclerosus et Atrophicus.—At a meeting of the Minnesota Dermatological Society during the summer of 1940, Becker presented a male patient aged 52 who had typical papules of lichen sclerosus et atrophicus in the clavicular and scapular regions, on the shaft of the penis and on the scrotum and the characteristic sclerosing lesions of balanitis xerotica obliterans on the prepuce and on the glans. Urethral stenosis was present. Unfortunately a biopsy was not performed on the glans, although the histologic picture of a lesion from the clavicular region was that of lichen sclerosus et atrophicus. Fabry,[27] in 1928, described a case in which, in all probability, there was a similar association. The patient, who was 35 years of age, was said to have had kraurosis penis complicated by a superficial carcinoma of the glans and "white spot disease" on the scrotum. Judging from the photomicrograph

24. Pautrier, L. M., and Camus, R.: Sclérodermie annulaire du gland, Bull. Soc. franç. de dermat. et syph. **39**:304 (Feb.) 1932.

25. Gougerot, H.; Degos, and Roulle, S.: Sclérodermie de l'anneau préputial, Bull. Soc. franç. de dermat. et syph. **41**:896 (June) 1934.

26. Gougerot, H., and Basset, A.: Sclérodermie en deux anneaux concentriques du gland et du sillon balano-préputial, Bull. Soc. franç. de dermat. et syph. **46**:1326 (Sept.-Oct.) 1939.

27. Fabry, J.: Ueber einen Fall von Kraurosis penis bei gleichzeitigem Bestehen von Weissflecken am Skrotum, Dermat. Wchnschr. **86**:7 (Jan. 7) 1928.

in the article, we believe the condition was an example of lichen sclerosus et atrophicus. The association in Becker's and in Fabry's patients affords interesting speculation concerning the relation of balanitis xerotica obliterans and lichen sclerosus et atrophicus. Is the former a manifestation of the latter localized to the penis or is such an association coincidental? Certainly the simultaneous occurrence of the two diseases must be extremely rare, or it would have been reported previously in the literature.

The characteristic lesion of lichen sclerosus et atrophicus is an irregular, often polygonal, flat-topped papule. The ivory or mother-of-pearl color of the lesions is striking. They may be discrete or may coalesce to form plaques, but in most cases both types of lesions are present. The presence of dells and of follicular plugging is regarded as an important diagnostic aid. It is noteworthy, however, that on the vulva the striking lesion is the plaque, although individual papules with dells or plugs may be seen at the periphery of the plaque. In the recent, thorough study of lichen sclerosus et atrophicus by Montgomery and Hill [28] the disease occurred in males in only 8 of 46 cases. Penile lesions were present in only 1 case, and these were characteristic papules located on the shaft. No mention was made of lesions simulating balanitis xerotica obliterans, as were observed in Becker's case. Both diseases, of course, are rare on the male genitals. If they were the same it would seem that a more frequent simultaneous occurrence of genital and body lesions should have been recorded. In none of our cases have we noted individual papules suggesting lichen sclerosus et atrophicus at the borders of the plaques characterizing balanitis xerotica obliterans, nor have the patients complained of lesions elsewhere on the body. Unfortunately, in most cases no careful search for other lesions was made, and unless such an examination were done, it would be easy to overlook small asymptomatic papules or patches of lichen sclerosus et atrophicus on the body when attention was focused on the genital lesions which were causing urethral stenosis and resulting disturbances of urination.

The histologic picture of lichen sclerosus et atrophicus shows a band of sclerosis in the upper part of the cutis. Even if this amount of sclerosis were insufficient to cause atresia and stenosis of the vagina when the disease occurred in the female, it might conceivably produce stricture of a much narrower orifice, such as the urethral meatus in the male. We are unable to decide whether or not balanitis xerotica obliterans and lichen sclerosus et atrophicus are the same disease. Certainly there is a close clinical and histologic similarity. When two related conditions occur at various ages, are similar clinically and even indistinguishable

28. Montgomery, H., and Hill, W.: Lichen Sclerosus et Atrophicus, Arch. Dermat. & Syph. **42**:755 (Nov.) 1940.

histologically, it seems difficult to separate them clearly when the lesions are limited to the penis.

D. Lichen Planus.—It is not within the scope of this paper to discuss the possible relation of lichen planus to lichen sclerosus et atrophicus, except to state that recent studies of the subject (Nomland,[29] and Montgomery and Hill [28]) strengthen the belief that the two are separate entities. Lesions of lichen planus limited to the penis may present a superficial similarity to balanitis xerotica obliterans. We have never observed the two conditions in 1 patient, nor to our knowledge has such an association been reported in the literature. If the characteristic lesions of lichen planus can be found elsewhere on the skin or mucous membranes, the diagnosis of the penile lesions presents no difficulty. Lesions of lichen planus on the genitals are more apt to be elevated in contrast to the atrophic plaques of balanitis xerotica obliterans, and urethral stenosis is not present in the former. In typical cases of the two diseases histologic studies also afford a reliable means of differentiation. Except in the rare atrophic forms of lichen planus there is an increase in the stratum corneum and stratum granulosum with varying degree of acanthosis, in contrast to distinct atrophy in balanitis xerotica obliterans. The sharply limited band of infiltrate in the upper part of the cutis in lichen planus persists even in the atrophic form of the disease, in which the epidermis is decidedly thinned. In cases of balanitis xerotica obliterans the area which is the site of the infiltrate in lichen planus appears edematous and homogenized. In 1 of our cases a moderate degree of infiltrate was noted high in the cutis, but the homogenized edematous papillary layer was present nevertheless, a feature which is not observed in lichen planus.

E. Kraurosis Penis.—One who carefully analyzes and compares the clinical and histologic features of balanitis xerotica obliterans and kraurosis penis is forced to admit that there are no essential differences. Both are chronic, atrophic, sclerosing processes of the prepuce and glans leading to urethral stenosis. Both show atrophy of the epidermis, edema and homogenization of the cutis, inflammatory changes about the blood vessels and diminution or loss of the elastic tissue. Stühmer admitted that the fundamental changes in the two diseases were the same but stated the belief that balanitis xerotica obliterans should be set aside as a separate entity because (1) it occurred in younger patients, (2) it followed some operative procedure and (3) the annoying itching and paresthesias which presumably characterize kraurosis penis were not prominent features in this disease. As we have stated previously, the aforementioned differential points seem insufficient, since balanitis xerotica obliterans has, since Stühmer's report, been observed in older

29. Nomland, R.: Lichen Sclerosus et Atrophicus (Hallopeau) and Related Cutaneous Atrophies, Arch. Dermat. & Syph. **21**:575 (April) 1930.

persons and in patients who have had no operation. Moreover, Delbanco reported kraurosis penis in patients as young as 39. We have noted annoying itching and paresthesias in several of our patients for whom we have made a diagnosis of balanitis xerotica obliterans. Such symptoms vary considerably and certainly do not carry a great degree of diagnostic significance. As Beek noted, carcinoma has been reported in cases of a condition diagnosed as kraurosis penis as well as in those of a disease called balanitis xerotica obliterans. In view of the rarity of such cases, regardless of title, the tendency to malignant change offers no reliable means of differentiation. We share the opinion of Beek that balanitis xerotica obliterans and kraurosis penis are identical. They look the same; the histologic pictures show no important variations; they follow the same chronic course, and both eventuate in urethral stenosis. Beek felt that kraurosis (or, as he termed it, progressive atrophy of the glans and prepuce) might be divided into the three following types: (1) spontaneous (Delbanco), (2) postoperative (Stühmer) and (3) postbalanitic (Grütz).

F. Leukoplakia Penis.—If the term leukoplakia is reserved for patchy, circumscribed, thickened, smooth or rough, milky, opalescent plaques which rarely occur on the glans or prepuce, there is less confusion with balanitis xerotica obliterans. Leukoplakia of the male genitals is identical with that occurring in the mouth. It is a hypertrophic, hyperplastic process rather than an atrophic retractive one. It may occur alone, as in Benedek's case, or in conjunction with atrophic lesions, as in the cases of Kraus and Genner and Nielsen. The same frequent association of kraurosis and leukoplakic vulvitis in the female has been emphasized by Montgomery, Counseller and Craig.[30]

Summary.—Even though it is not possible to say that leukoplakia, balanitis xerotica obliterans, scleroderma and lichen sclerosus et atrophicus are the same, they must stand in close relation to one another. Kraurosis penis and balanitis xerotica obliterans seem to us indistinguishable; we have observed lichen sclerosus et atrophicus of the body and balanitis xerotica obliterans in the same patient. Touraine noted balanitis xerotica obliterans and morphea in the same patient, and leukoplakia and atrophic changes have been frequently seen together in both male and female. In all probability there is some unknown property of the tissues of certain persons which predisposes them to the development of these various sclerosing processes. In our opinion there is insufficient evidence to conclude that leukoplakic (hypertrophic) changes occur primarily in balanitis xerotica obliterans and that atrophy develops later. It seems more likely that the two conditions occur coincidentally, since they are the exact opposite of each other histologically.

30. Montgomery, H.; Counseller, V. S., and Craig, W. M.: Kraurosis, Leukoplakia and Pruritus Vulvae, Arch. Dermat. & Syph. **30**:80 (July) 1934.

COMMENT

The cause of balanitis xerotica obliterans is unknown. In his original presentation Stühmer opined that the most important factor in the pathogenesis was circumcision, which led to a mechanical disturbance and an unusual drying of the glans. These factors predisposed to subsequent inflammation or infection which finally brought about sclerotic changes characterizing the fully developed condition. He was unable to incriminate any specific organism. He felt that there were initial acanthosis and hyperkeratosis as a result of these epidermal insults and that the changes in the cutis were secondary. It is obvious that circumcision does not necessarily precede balanitis xerotica obliterans, since in many cases there has been no previous operation, and, conversely, balanitis xerotica obliterans has not followed countless circumcisions. Since Stühmer's publication, other authors, including Grütz, Beek and de Gregario, de Blasio and Hijar, have suggested that the atrophic and sclerotic changes of balanitis xerotica obliterans are the consequence of a chronic inflammatory state induced by repeated attacks of balanoposthitis provoked usually by partial or total phimosis. Various bacteria, such as streptococci, streptobacilli and spirilla, have been found on the genitals but were not regarded by the observers as etiologically important. The disease is unrelated to syphilis or other systemic diseases. One of Grütz's patients had diabetes, although adequate studies of 2 other patients showed no signs of the disease.

The therapy of well developed balanitis xerotica obliterans is difficult, since restitution of the sclerotic parts to normal by any known therapeutic means cannot be expected in most cases. Stühmer said that the application of bland emollient ointments following circumcisions was of prophylactic value and that similar therapy early in the course of the disease might retard its progress. De Gregario, de Blasio and Hijar expressed the opinion that the early circumcision of all patients with phimosis would help to avoid the repeated attacks of balanoposthitis which in turn create a chronic inflammatory state leading to balanitis xerotica obliterans.

Once the disease is fully developed the chief consideration is the maintenance of a urethral opening of adequate size so as to prevent retention of urine. The most common procedure is to pass sounds repeatedly and as frequently as the condition of the meatus demands. Gayet expressed the belief that more radical therapy should be done, stating that rapid recurrence of the urethral stenosis followed even meatotomy and that a veritable hypospadias should be surgically created to insure a permanently adequate orifice and avoidance of serious damage to the urethra, bladder and kidneys. We do not share this view. Such complications did not develop in any of our patients in spite of extreme narrowing of the meatus. It is the consensus that any operative treat-

ment of stricture may aggravate the condition. Furthermore, it is our distinct impression that the entire process in balanitis xerotica obliterans improved in some instances after the repeated passage of bougies, the improvement perhaps being analogous to that obtained by massage in scleroderma. It is our opinion that routine dilation of the urethra at regular intervals (at least monthly) by means of bougies is important in the management of this disease. In cases characterized by a constricting band about the prepuce, circumcision adds greatly to the comfort of the patient, and in 1 of our cases there was remarkable improvement of the entire process within three months after such an operation.

SUMMARY AND CONCLUSIONS

1. Balanitis xerotica obliterans is a chronic, progressive, atrophic, sclerosing process of the glans and prepuce leading to urethral stenosis.

2. Operations on the genitals are unnecessary for its development, and it may occur in adults of all ages.

3. The histologic picture consists of atrophy of the epidermis, edema and homogenization of the papillary cutis, perivascular inflammatory changes and diminution or loss of the elastic tissue.

4. In our opinion kraurosis penis and balanitis xerotica obliterans are the same disease, since insufficient clinical and histologic differences exist to permit their separation.

5. Further observations are necessary to decide the relation of balanitis xerotica obliterans and lichen sclerosus et atrophicus. If not identical, they are extremely closely allied.

6. Scleroderma can be differentiated from balanitis xerotica obliterans on histologic grounds. Scleroderma of the penis is extremely rare.

7. The term leukoplakia of the penis should be reserved for hypertrophic rather than atrophic lesions.

8. The therapy of balanitis xerotica obliterans must be directed toward the maintenance of an adequate urethral meatus by means of the regular passage of dilating bougies.

ABSTRACT OF DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: Drs. Freeman and Laymon have made a good case for considering this condition a variant of kraurosis penis and possibly an entity. They have elaborated on the differentiation of this condition from lichen sclerosus et atrophicus, scleroderma and leukoplakia. I wish to report observations that correspond to those presented by the authors.

The patient was under observation for six years. When first seen, he was 62 years of age and stated that he had had a dorsal slit performed a year and one-half before the development of his penile lesions. This was done because of an acquired phimosis, which was apparently associated with a balanitis. His first lesions were apparently unrelated to this surgical procedure, although such

an operation has been indicated as a possible cause of the disease in some cases. The first lesion was on the glans about the meatus and was in its early stage an edematous and inflammatory plaque showing the telangiectasia resembling radiodermatitis to which Dr. Laymon referred. Subsequent to this several lesions developed on the prepuce which became bandlike infiltrates like those discussed. The lesions later became atrophic, but before the stage of atrophy was reached an acute urinary retention developed because of the inflammatory infiltrate and edema about the meatus. A meatotomy was performed, with permanent relief. At that time material taken from the meatus for biopsy showed the characteristic pathologic changes that Dr. Laymon has described, which appear to aid in the differentiation of this disease from the other diseases discussed.

Dr. Harold N. Cole, Cleveland: I have had a few cases of this kind in private practice, and I suppose I have probably encountered half a dozen that have been presented at meetings of the Cleveland Dermatological Society. I do not think there is any relation between this process and surgical procedures. In line with the viewpoint that this condition really is similar to kraurosis vulvae, I should certainly recommend the use of injections of estrone (theelin) and should be inclined to think that it would have a beneficial effect on the condition.

Dr. C. Guy Lane, Boston: I was interested in Dr. Laymon's differentiation between this condition and lichen sclerosus because of a recent case of mine which is in all probability one of lichen sclerosus.

A man of 35 had two lesions, with gradual onset, one on the prepuce as a white sharply outlined band and the other covering the tip of the penis as if a tight cap of white celluloid were placed over the tip of the glans, with some slight shrinkage of the urethral opening. The lesions had appeared gradually, with no symptoms, over a period of perhaps two years. A circumcision was performed. After a tentative diagnosis was made of either lichen sclerosus or scleroderma, the section was reviewed by Dr. Hill, who had been working with Dr. Montgomery, and he concluded that the histologic picture was fairly characteristic of lichen sclerosus.

Dr. Joseph Victor Klauder, Philadelphia: I should be inclined to go further in the visualization and classification of this disease than have Drs. Freeman and Laymon. There is a clinical similarity between balanitis xerotica obliterans and ocular pemphigus. In the latter disease there is a slowly progressive inflammatory process characterized by xerosis, the formation of adhesive bands (symblepharon) traversing the conjunctiva, ending in obliteration of the conjunctival sac, and the formation of a parchment-like membrane covering the cornea, causing blindness. Cicatrization and obliteration of opposing mucous surfaces occurs in pemphigus of the mucous membrane, of which ocular pemphigus is one phase. In patients with pemphigus of the mucous membrane who may or may not have ocular involvement, there occurs, for example, atresia of the vagina, stenosis of the esophagus and obliteration of the nasopharynx and of the space between the buccal mucosa and the alveolar process. In some cases of balanitis xerotica obliterans there is involvement of the mucous membrane of the anus. It is to be recalled that this occurred in 1 of the several patients with this disease presented at the clinical meeting of the International Congress of Dermatology, Copenhagen, Denmark. It is pertinent to examine all mucous surfaces of patients with balanitis xerotica obliterans.

In a paper (Klauder, J. V., and Cowan, A.: Ocular Pemphigus and Its Relation to Pemphigus of the Skin and Mucous Membranes, *Am. J. Ophth.*, to be published) mention was made of Traub's patient with ocular pemphigus who

also presented lesions on other mucous surfaces, including the glans and sulcus, eventuating in adherence of the foreskin to the glans.

In so far as concerns cicatrization, fusion and obliteration of opposing mucous surfaces, the two diseases are comparable. In pemphigus of the mucous membranes, however, the process may attack one or many mucous surfaces, whereas in balanitis obliterans it is invariably localized. Vesicles to my knowledge have never been reported as occurring in balanitis obliterans, whereas they are conspicuous in pemphigus of the mucous membranes but considerably less conspicuous when the disease affects the conjunctiva (ocular pemphigus).

DR. SAMUEL E. SWEITZER, Minneapolis: I think the interesting feature of this paper is that it is a report of a disease that has not been written up in America. In Minnesota there was a group of 18 cases. Proof of the practical identity of the disease with kraurosis penis and its close association with lichen sclerosus et atrophicus are items in the paper that appealed particularly to me. Stühmer emphasized that the condition was caused by circumcision or had had some connection with it. The last patient with the condition I had in my clinic was an old man who also had coronary disease, from which he later died. He had a condition of the prepuce similar to the one described here. My assistant performed a circumcision and a meatal dilation. In this case, as in numerous others, the prepuce was involved with a thick band and caused almost as much trouble as the meatal involvement.

DR. CHARLES FREEMAN, St. Paul: One of our purposes in writing this paper was to stimulate the study of this condition and, if possible, to place it definitely. I think it is well named. The balanitis, the xerotic condition and also the obliterating of the meatus are present. If it is not an entity it is at least an oddity.

We realize that two of our investigations are not exactly complete. I think we were amiss in not carefully examining the entire body for other than penile lesions. But even in the patients that we did examine none were found. I think one may be partially excused by the fact that one's attention may be diverted because the predominating symptom is the difficulty of urination. Another regrettable fact was our inability to get a biopsy specimen from Dr. Fred Becker's patient who was shown before the Minnesota Dermatological Society (ARCH. DERMAT. & SYPH. **43**:430 [Feb.] 1941). He had lesions of lichen sclerosus et atrophicus on the body and also partial stenosis of the urethral meatus. Because of this I suggest that in all cases of this nature the patient be carefully scrutinized.

Dr. Laymon and I are of the opinion that balanitis xerotica obliterans closely simulates kraurosis, both clinically and histologically, and that scleroderma, leukoplakia and variants of lichen planus may be reasonably ruled out.

We are definitely sure that Stühmer's contention that balanitis xerotica obliterans follows circumcision is a false premise, as circumcision played little or no role in any of our cases.

As has been mentioned, the only treatment that has been of any value is dilation of the urethral meatus.

One discusser mentioned the administration of estrogen. I know this has been tried in kraurosis vulvae without any spectacular result.

Dr. Klauder spoke of pemphigus as a causative factor. This possibility never occurred to us at all.

MEMBRANOUS STOMATITIS ASSOCIATED WITH DEBILITATION AND WITH UREMIA

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BALTIMORE
AND
HARRY KEIL, M.D.
NEW YORK

The concept of membranous stomatitis includes a host of conditions characterized by the formation of a membranous deposit in one or more areas in the oral cavity. When a definite etiologic agent can be identified (Bacillus diphtheriae, Vincent's organisms or Spirochaeta pallida) or when the lesions can be classified within a circumscribed category (pemphigus or erythema multiforme exsudativum), the specific term membranous stomatitis may be applied in a general way. There are, however, numerous other ill defined membranous lesions in the mouth about which present knowledge is scanty in practically all particulars, especially in their histologic aspects. It is with a view to the clarification of this heterogeneous group of conditions that the present report is written.

Pathologists differentiate a pseudo membranous inflammation (membrane formed chiefly of exuded inflammatory fibrin) from a true membranous deposit (membrane consisting only of coagulated or necrotic epithelium). In practically all examples of stomatitis the membranous deposit belongs in the first category (pseudo membranous inflammation), whereas a possible example of true membranous inflammation is that observed in agranulocytic angina. While we recognize the justification for this distinction, we are nevertheless retaining the term membranous stomatitis for the fibrinous deposits seen in our 2 cases because this term has received wide clinical acceptance and because it is often difficult to make absolute distinctions.

MEMBRANOUS STOMATITIS ASSOCIATED WITH DEBILITATION

CASE 1.—J. S., a white woman aged 22, sustained a compression fracture of the eleventh dorsal vertebra, resulting in paraplegia from the waist down, loss of motor and sensory power below this level and incontinence of feces and urine. She lost weight rapidly. There appeared decubital ulcerations, progressive cachexia

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and a secondary anemia that gradually became more pronounced (the hemoglobin diminished from 84 to 54 per cent). Examination of the urine revealed a 2 plus reaction for albumin, with 50 to 75 white blood cells per high power field. The blood urea nitrogen amounted to 9.2 mg. per hundred cubic centimeters and the blood sugar to 103 mg. At one time she complained of pain and soreness of the mouth. The tongue was red and somewhat beefy, and there were many small white plaques scattered over the buccal mucosa. These lesions regressed for a time under treatment with tincture of myrrh.

Three months later there appeared on the under surface of the tongue and extending to the floor of the mouth a thick white, elevated, smoothly glistening membrane composed of coalescent smaller patches showing in places a fine erythematous border. The membrane could be easily detached but left a raw,

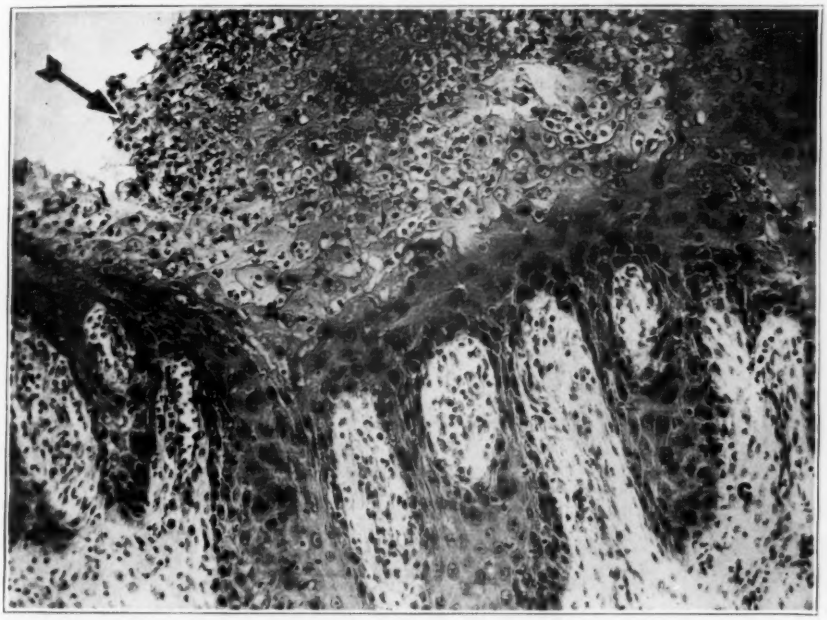

Fig. 1 (case 1).—The arrow points to the edge of the fibrinous membrane. *A*, area of necrotic epithelium; *B*, acanthotic pegs; *C*, young fibroblastic proliferation.

bleeding surface. Smears showed gram-positive cocci in pairs and short chains. A culture revealed a predominant growth of Staphylococcus aureus with some colonies of Streptococcus anhaemolyticus (gamma). Another culture, made three weeks later, disclosed Str. anhaemolyticus as the predominant organism, together with Staphylococcus albus and Micrococcus catarrhalis. Repeated mycologic examinations showed no fungi. The lesions coalesced gradually and showed no therapeutic response to the application of gentian violet. Histologic examination of a piece of membrane revealed dense fibrinous material infiltrated superficially and deeply with polymorphonuclear leukocytes, suggesting an acute inflammatory process extending into the depth of the tissue.

Under the topical application of essence of caroid (a preparation of papaw), the lesions regressed almost completely, but a recurrence of the process appeared

shortly before death. The entire clinical course from the date of the accident was but ten months.

The following observations were made on postmortem examination: transection of the spinal cord at the eleventh dorsal vertebra, decubital ulcers, chronic cystitis, hepatosplenomegaly and pericardial effusion. Examination of the kidneys revealed no significant abnormalities, either grossly or microscopically.

At necropsy tissue was removed from the under surface of the tongue. Histologic examination showed an exudate composed of fibrin, polymorphonuclear leukocytes and necrotic epithelium occupying areas of mucosal surface. The epithelium was in places irregularly acanthotic. In the submucosa there was evidence of a reparative process in the form of granulation tissue, featured chiefly by a proliferation of young fibroblasts and a moderate number of new capillaries (fig. 1). The superficial portion of the underlying musculature showed irregular atrophy of muscle fibers, but this process was not pronounced. In the deeper portion of the musculature were areas containing groups of proliferating sarcolemma nuclei, probably a reaction to the neighboring inflammation in the tissue (fig. 2). The

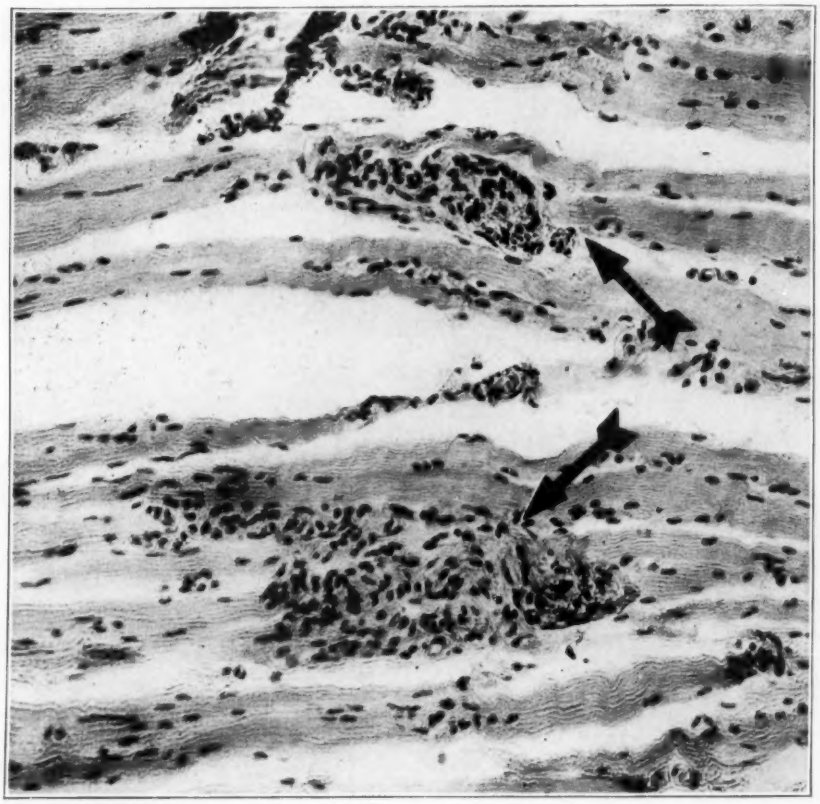

Fig. 2.—A deeper portion of the section shown in figure 1. Arrows point to areas of proliferation of sarcolemma nuclei. The muscle bundles show no definite abnormalities.

depth of the pathologic process was noteworthy when one considers that the enanthem had seemed fairly superficial on clinical examination.

The peculiar appearance presented by the lesions in the floor of the mouth and on the inferior aspect of the tongue, especially the smooth and glazed surface, was striking. Consultation with the members of the dental department revealed that this manifestation was not a familiar one.

A review of the literature failed to disclose any records of cases analogous to ours. Of all the oral conditions mentioned, the closest seemed to be the uncommon one classed as nonspecific membranous stomatitis. Examples of this, probably a disease of heterogeneous clinical features, have been recorded by Hiller,[1] Cahn [2] and Thoma.[3] These few examples, however, were a form of membranous stomatitis of acute or subacute course occurring in apparently healthy persons; the eruption was composed of discrete smaller patches surrounded by a more pronounced erythematous border and showing a tendency to coalesce; the enanthems appeared at various sites in the oral and pharyngeal mucous membranes, and the response to therapeutic agents was usually successful. The points of similarity with the condition in our case were that mycologic examinations revealed no fungi and cultures revealed a predominance of the different members of the streptococcic and staphylococcic groups of organisms, with a sprinkling of other bacteria, such as diphtheroids, pneumococci and M. catarrhalis.

Our case, on the other hand, was that of a debilitated patient in whom the lesions, though responding at first to essence of caroid, were essentially chronic and resistant, probably owing to the cachectic state. It is likely that in such a person food may accumulate beneath the tongue and provide in this way a predisposing factor to infection, with multiplication of whatever organisms happen to constitute the flora at that time. It is, however, striking that the predominant organisms belonged to the streptococcic or staphylococcic group, whereas Bacillus fusiformis and Vincent's spirochete were absent; this may perhaps be due, in part at least, to the anatomic localization. The histologic examination showed that, at least in the late stages of the process, the infection involved deeper tissue than the clinical attributes led us to believe. That this condition is probably more common than is generally supposed is indicated by our recent observation of a similar enanthem on the floor of the mouth and on the inferior surface of the tongue in a case of ulcerative colitis. We believe that oral prophylaxis is of the utmost necessity in cases of this sort.

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1. Hiller, B.: Membranous Oropharyngitis, M. J. Australia **2**:649, 1935.

2. Cahn, L. R.: Nonspecific Membranous Stomatitis, Internat. J. Orthodontia **22**:869, 1936.

3. Thoma, K. H.: Membranous Stomatitis Nonspecific: Case, Internat. J. Orthodontia **23**: 404, 1937.

MEMBRANOUS STOMATITIS ASSOCIATED WITH UREMIA

CASE 2.—A. N., a white man aged 22, entered the hospital for an illness that began eighteen months before admission. He had a congenital median bar of the prostate with obstruction resulting in chronic cystitis and ureteritis, pyelonephritis, chronic uremia, hypertension (systolic 190 and diastolic 130) and evidence of cardiac failure. Previously a left nephrectomy had been done, and subsequently a right pyelostomy, after which the urea nitrogen content of the blood rose from 100 to 175 mg. per hundred cubic centimeters and the creatinine from 2.8 to 15.6 mg. A pronounced secondary anemia was present. The course was downhill, and the condition was associated with itching, occasional nausea and vomiting, and twitchings of the body.

Ten days before death dirty gray ulcerations appeared on the surface of the tongue and on the floor of the mouth. The lesions were partly discrete and partly coalescent. A small discrete lesion was also present on the buccal gingiva of the left side. The membrane could be lifted off easily, leaving a raw oozing, superficially eroded area which bled profusely and over which the membrane recurred

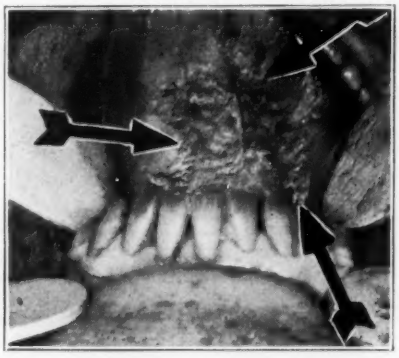

Fig. 3 (case 2).—The appearance of the lesion on the under surface of the tongue after detachment of most of the membrane. Arrows circumscribe the altered mucous membrane, which in places shows clinically what seems to be superficial necrosis.

in from twenty-four to forty-eight hours. The patient complained of severe pain in the mouth, especially on mastication. The clinical features were those of uremic stomatitis. Smears showed a predominance of gram-positive bacilli with some gram-negative bacilli. On culture Bacillus proteus and B. diphtheriae were isolated. Mycologic cultures were sterile. Histologic examination of the membrane revealed some fibrinous material, necrotic epithelium penetrated by an infiltration of disintegrating polymorphonuclear leukocytes and numerous clumps of bacteria in the superficial portion of the tissue.

At necropsy the clinical diagnoses were substantiated, and a specimen of the inferior surface of the tongue was removed for further study (fig. 3). On histologic examination this tissue was found to be the site of an intensely acute process. There was extensive necrosis of the entire area of involved mucosa with an exudate composed of polymorphonuclear leukocytes in various stages of decomposition, together with fibrinous material. The submucosa was edematous

and infiltrated by a similar exudate (fig. 4). The immediately subjacent muscle showed edema of the muscle bundles with cloudy swelling, haziness of the cross striations, occasional loss of all striations and fragmentation. In the deeper portion of the muscle there was irregular atrophy of the muscle bundles with replacement fibrosis and occasional proliferation of sarcolemma nuclei; there was no evidence of an acute inflammation in this area (fig. 5).

Uremic stomatitis as an entity has been known for the past half-century,[4] and additional clinical descriptions have been recorded by a few observers.[5] The clinical attributes of this form of stomatitis, as exemplified by the condition in our case, are: (1) an apparently superficial type of acute ulcerative stomatitis covered by a whitish membrane,

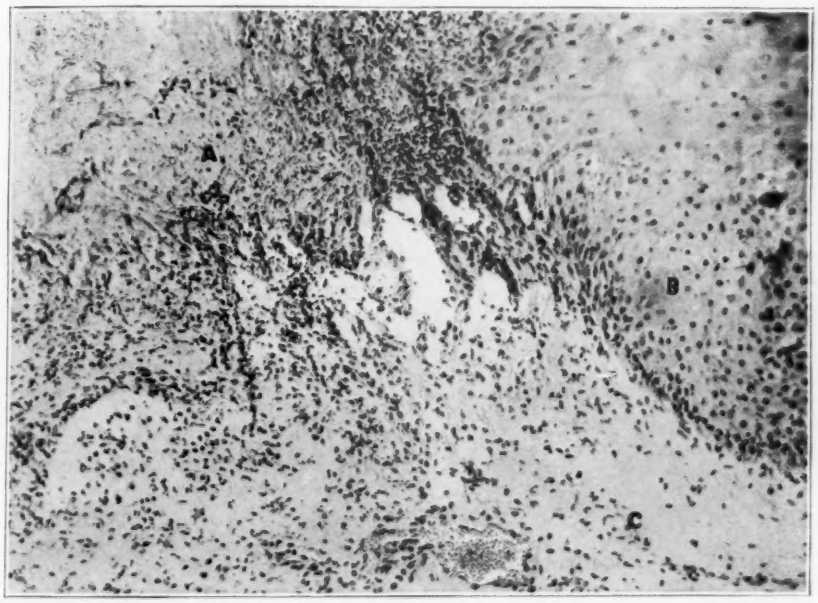

Fig. 4.—Section from the altered area shown in figure 3. *A*, the necrotic pseudomembrane; *B*, a swollen rete peg at the extreme edge of the necrotic mucous membrane; *C*, the swollen, edematous and infiltrated submucosa.

4. Lancéreaux, M.: Anatomie pathologique et complications de l'urémie, Union méd. **44**:829, 1887. Barié, E.: De la stomatite urémique, Arch. gén. de méd. **2**: 415, 1889.

5. (*a*) Hertz, E.: Les stomatites urémiques et leur diagnostic, Semaine méd. **22**: 109, 1902. (*b*) Dalché, P., and Claude, H.: Ulcérations hémoragiques de la peau et des muqueuses dans l'urémie, Bull. et mém. Soc. méd. d. hôp. de Paris **20**:75, 1903. (*c*) Chargin, L., and Keil, H.: Skin Diseases in Nonsurgical Renal Disease, Arch. Dermat. & Syph. **26**:314 (Aug.) 1932. (*d*) Abascal, M. P., and Echeverría, B. J. I.: Uremic Stomatitis, Rev. méd. d. Uruguay **29**:1, 1926; cited by Hempstead and Hench. (*e*) Hempstead, B. E., and Hench, P. S.: Uremic Stomatitis, Tr. Am. Laryng., Rhin. & Otol. Soc. **36**:510, 1930.

removal of which exposes a raw surface and which rapidly reforms; (2) severe subjective symptoms, such as pain, foul odor and salivation, and (3) occurrence in the terminal stages of uremia. There is reason to believe that, as in the case of involvement of the gastrointestinal tract and the skin, the oral manifestations represent the result of an abortive attempt to compensate for the retention of the hypothetic substance or substances retained in renal failure. The lesions in the mouth (and also in the pharynx) are probably analogous, then, to the intestinal ulcerations

Fig. 5.—A deeper portion of the section illustrated in figure 4. The arrow points to an area of replacement fibrosis. There are irregular atrophy of muscle and a slight tendency toward proliferation of the sarcolemma nuclei.

so commonly encountered in cases of uremia. However, in our case the postmortem examination revealed a comparative freedom from the latter complication. On the other hand, pruritus was present toward the end of the clinical course.

Chargin and Keil [5e] pointed out that an apparently similar form of stomatitis may occur with various types of nephritis in the absence of azotemia, and they attributed these lesions to a probable lowered tissue resistance. The oral manifestations of this type of disease usually lacked

the severity of the enanthem in uremia, responded readily to treatment and had a good prognosis. Further investigation of this type of stomatitis unaccompanied by azotemia seems desirable, particularly its relation, if any, to the uremic type.

Knowledge of the histologic changes in cases of uremic stomatitis is meager. The literature contains the reports of but 3 instances [6] in which such studies were pursued, and it is evident from the descriptions that the specimens for biopsy were taken usually from the superficial tissues. Hempstead and Hench,[5e] summarizing the pathologic features in their 2 cases, found that the superficial layers of mucosa were so deeply destroyed that the tops of the papillary bodies were exposed and only the tips of the rete pegs remained. There were a moderate amount of leukocytic migration through the vessels in the papillary bodies, occasional thrombosis of the vessels in the submucosa and evidence of endothelial proliferation. The superficial exudate was structureless and the cellular remains indistinct. Bacteria were abundant but not identified. In our case we were able to secure a specimen which included deeper muscle as well and, in addition to the aforementioned description, which we can confirm in its essentials, we found involvement of the subjacent muscle to a considerable depth. These alterations were not due directly to the acute superficial inflammation but rather represented a distant reaction to the overlying process, with probable diffusion of "toxins" capable of damaging the muscle bundles, leading to atrophy and in some areas replacement fibrosis. There was no evidence in our sections that the muscular changes could be attributed to primary vascular closure.

The organisms found in the membrane in our case were identified as B. proteus and B. diphtheriae; of these the former would appear to be the more significant. It has been pointed out [5c] that Vincent's organisms are commonly found as secondary invaders in instances of uremic stomatitis. In our case smears failed to disclose these organisms.

SUMMARY

Two examples of various types of membranous stomatitis are recorded. The first was associated with a state of chronic debilitation and the other with uremia. The clinical attributes of each are described in detail. This study may be considered as preparatory to the classification of types of so-called membranous stomatitis, a vague and ill defined disease.

The histologic structure observed in a case of membranous stomatitis associated with debilitation is recorded for the first time. The anatomic observations of this variety are those of a subacute inflammation with

6. Abascal and Echeverría.[5d] Hempstead and Hench.[5e]

formation of fibrin and evidence of repair. In uremic stomatitis, however, the process is more acutely necrotic, and in the degree of epithelial necrosis the pathologic features seem to stand midway between what pathologists call pseudo membranous inflammation and true membranous inflammation. In our 2 cases biopsy specimens showed that the muscle fibers were affected, though far more severely in uremic stomatitis. This probably occurs as an indirect consequence of the more superficial inflammation.

Cultural details are furnished in both cases. It seems interesting to note that Vincent's organisms were not present. The significance of the apparently banal cultural findings is briefly discussed.

The occurrence of membranous stomatitis on the inferior surface of the tongue and in the floor of the mouth is, in general, to be regarded as a probable indication of the local growth of the oral flora or the accumulation of the various "toxic" products. This statement refers to chronic membranous stomatitis of the types herein recorded and not to various other forms of acute stomatitis in which this localization sometimes occurs in an accidental fashion.

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PHOTODYNAMIC ACTION OF LIME OIL (CITRUS AURANTIFOLIA)

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During the past two decades an increasing number of reports have been made concerning photodermatitis which is produced by topical application on the skin of certain plant substances and subsequent exposure of the skin to sunlight. The supposed offending agent was either an aromatic oil or some part of the oleoresinous content of the plant which came in contact with the skin. Perhaps the earliest and the commonest example is now referred to as Berlock dermatitis, which was first reported by Freund [1] in 1916. This followed the application of certain toilet waters and perfumes and subsequent exposure to sunlight. It is alleged to be due in part to bergamot oil and occasionally to certain other essential oils also present in the preparations. Ten years later Oppenheim [2] called attention to an eruption which occurred in persons taking sun baths who were at the same time in contact with certain meadow plants. He subsequently named the condition dermatitis bullosa striata pratensis, and since that time numerous reports on its appearance and the mechanism of its production have been published. Kitchevatz [3] published a series of papers during the past decade describing in one a photocatalytic dermatitis due to contact with figs and subsequent exposure to light.[3a] He thought the dermatitis was produced by solar radiation, particularly the red rays of the spectrum acting through an intermediary substance, the chlorophyll of figs, which rendered the skin more sensitive.[3b] Further studies on photodermatitis

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Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 7, 1941.

1. Freund, E.: Dermat. Wchnschr. **63**:931, 1916; cited by Gross and Robinson.[5]

2. Oppenheim, M.: Dermatite bullosa striée, consécutive aux bains de soleil lans les prés (Dermatitis bullosa striata pratensis), Ann. de dermat. et syph. **3**:1-7 (Jan.) 1932.

3. Kitchevatz, M.: (*a*) Etiologie et pathogénèse de la dermatite des figues. Note préliminaire, Bull. Soc. franç. de dermat. et syph. **41**:1751-1759 (Nov.) 1934; (*b*) Rôle sensibilisateur probable des dérivés de la chlorophylle et des colorants du sang, réglés d'apres différents longueurs d'ondes, ibid. **40**:764-765 (May) 1933; (*c*) Nouvilles récherches sur la photosensibilisation de la peau, ibid. **43**: 581-588 (March) 1936; (*d*) L'éclipse solaire du 19 juin 1936 et les recherches sur la photosensibilisation, ibid. **43**:1564-1568 (July) 1936; (*e*) Photodermite actino- calorique chlorophyllienne. Note preliminaire, ibid. **40**:761-764 (May) 1933.

produced by the fig have followed these reports. The agent causing the photodynamic action was not isolated, but it was concluded by the authors of a subsequent report [4] that chlorophyll was not the only agent concerned in the production of the reaction. They found the photosensitizing agent also in the latex of the fig (Ficus carica).

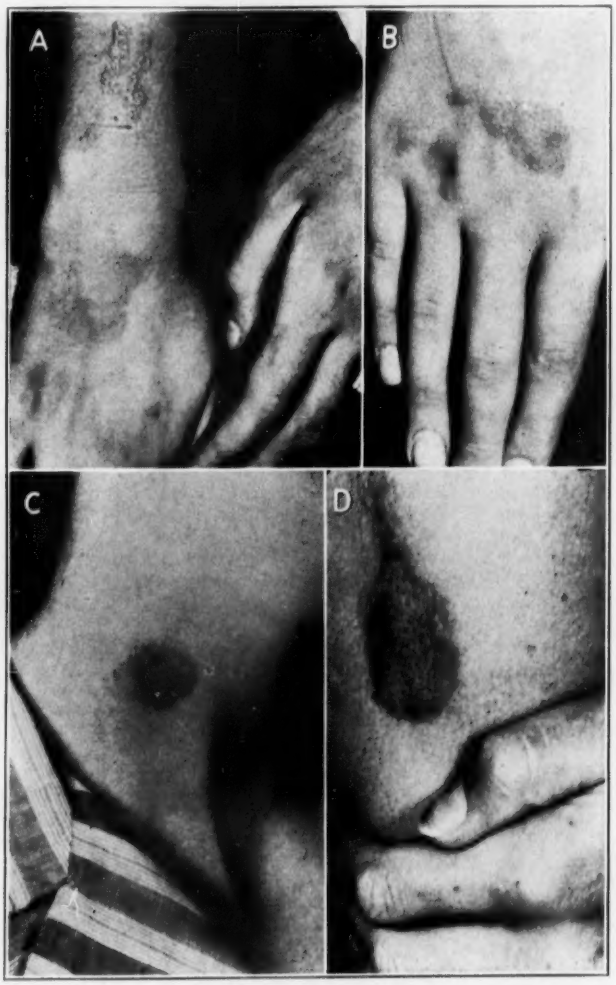

Fig. 1.—Pigmentation due to lime oil and subsequent exposure to the sun. *A* (case 2), pigmentation on the dorsum of the hand (the vesicular reaction on the wrist was experimentally produced); *B* (case 10), pigmentation on the dorsum of the hand; *C* and *D* (case 3), pigmentation on the neck, hand and elbow.

4. Behcet, H.; Ottenstein, B.; Lion, K., and Dessauer, F.: Les dermatites des figues; recherches des influences chimiques, physiques et allergiques pouvant provoquer la dermatite des figues, Ann. de dermat. et syph. **10**:32 (Jan.); 125 (Feb.) 1939.

The first report on bergamot dermatitis in this country was made by Gross and Robinson [5] in 1930. Cummer and Dexter [6] have reported photodermatitis resulting from contact with the gas plant (Dictamnus albus) and subsequent exposure to sunlight. They expressed the opinion that the photodynamic substance resided in the aromatic oil, but they failed to obtain reactions when an alcoholic extract, an ethereal extract and a water distillate were applied to the skin and the skin was subsequently exposed to sun.

In southern Florida there is an unusual opportunity to observe the effects of photodynamic substances. The number of available hours of sunshine is greater than in most sections of the country, and in a mild climate many residents avail themselves of the opportunity for sun bathing. During a period of seven years I have observed 44 cases of contact photodermatitis. The history and the location and the appearance of the dermatitis indicated bergamot oil as the probable offending agent in 25 cases. In 8 cases neither the history nor subsequent study disclosed the offending agent. In the remaining 11 cases I have been able to determine, either by history or by subsequent investigation, that the offending agent is oil from the Persian lime (Citrus aurantifolia, var. Swingle). The photodynamic nature of this agent was first suggested by the histories obtained from patients who presented themselves with a characteristic dermatitis usually on the hands or forearms or occasionally about the face. The following histories are typical of these 11 cases. In those not reported, the appearance of the eruption (fig. 1) and the history of handling limes and subsequent exposure to the sun are identical.

REPORT OF CASES

CASE 1.—Miss N. A. had an eruption on her hands and arms which began about July 4. Her mother was unable to assign any cause, but detailed questioning brought out the fact that the girl had attended a beach picnic on July 4. Before the picnic limeade had been made from Persian limes, and the patient had assisted in extracting the juice. She had not, so far as could be determined, used any perfume or toilet water, nor was there a history of contact with other cosmetics. Examination showed a hyperpigmented eruption involving the dorsa of the hands and fingers. It extended up on the wrists and the flexure surfaces of the arms and also occurred around the axillas and shoulders. The configuration and outline of the various lesions suggested that some liquid had been smeared on the skin in an irregular but at the same time artificial fashion, producing in some places rounded and in others square or straight lesions.

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5. Gross, P., and Robinson, L. B.: Berlock Dermatitis: Unusual Dermatitis and Pigmentation Following Use of Perfume, Arch. Dermat. & Syph. **21**:637-641 (April) 1930.

6. Cummer, C. L., and Dexter, R.: Dermatitis Caused by Dictamnus Albus (Gas Plant): Example of Photosensitization, J. A. M. A. **109**:495-497 (Aug. 14) 1937.

CASE 2.—Miss M. C. F. was under treatment for acne, and on one of the visits to the office it was noted that she had a brownish pigmentation over the dorsa of the hands, with the usual diffusion of pigmentation between the fingers. She had been squeezing Persian limes to make limeade and was well sun tanned.

The cortex of a Persian lime was broken, and the oil was rubbed on the dorsum of the left wrist. The wrist was then exposed to the sun for one hour (1:00 to 2:00 p. m.). A perceptible erythema was apparent in twenty-four hours. Vesiculation was present in seventy-two hours. This was followed by exfoliation and the appearance of a depigmented area surrounded by hyperpigmentation. Five months later a letter was received from this patient stating that the white area and the surrounding zone of hyperpigmentation had almost disappeared. At the time of the described experiment an area on the right wrist was treated with lime oil in a like manner. It was covered and not exposed to light, and no reaction of any type could be observed.

CASE 3.—A. B., a young girl, presented herself for examination five or six days after she had attended a Sunday school picnic. Limeade had been on the menu, and she assisted in its preparation. At the same time she had applied oil of citronella in order to keep off insect pests, and this was also considered as a possible cause of the dermatitis. She had an eruption made up of irregular, pigmented spots. One was on the left side of the neck, another in the left deltoid region and a third on the dorsum of the right hand, and at the same time there was diffuse pigmentation across the upper lip. Tests with oil of citronella and with lime oil were made, and erythema and subsequent pigmentation could be produced from limes but not from the oil of citronella. The distribution of the dermatitis can easily be explained by her attempt to defend herself from insect pests with her hands.

EXPERIMENTS

In the first case observed, in which the lime seemed to be the photodynamic agent concerned, testing failed to support the history elicited. This was due to the fact that attempts were made to produce the photodynamic action by the use of the artificial ultraviolet radiation from a quartz mercury vapor arc lamp. The studies by Jensen and Hansen [7] on the photodynamic substance of the parsnip (Pastinaca sativa) indicated that the active spectral range for the production of the photodynamic action was of a longer wavelength than that produced by therapeutic lamps in common use. Moreover, there seems to be a range of individual variation in sensitivity, and it was my unfortunate experience to attempt the first test on a subject who was relatively insensitive and in an area which had already been previously exposed to the sun. Both of these factors must be considered in attempting to reproduce experimentally the photodermatitis.

In the summer of 1938 there was an unusually large crop of Persian limes in the Dade County district of Florida. This citrus fruit is now

7. Jensen, T., and Hansen, K. G.: Active Spectral Range for Phytogenic Photodermatosis Produced by Pastinaca Sativa (Dermatitis Bullosa Striata Pratensis, Oppenheim), Arch. Dermat. & Syph. **40**:566-577 (Oct.) 1939.

grown on a commercial scale in this localized area and is used, as the histories would indicate, to make limeade, mixed drinks, salads, etc., the lime being similar to the better known lemon. At the Dade County Hospital, which is located near the fruit-growing district, I observed a number of cases of occupational dermatitis, in which there was pronounced pigmentation on the dorsa of the hands. According to the histories obtained from these workers, the hands would usually itch and burn and be red for a few days after they began to pick limes, and this erythema in a week or more would be followed by pigmentation, after which little additional irritation would ensue. Since the operation in progress at the time was chiefly picking, sorting and grading limes and not spraying, I considered that the plant oil, and not insecticides or fertilizers, was the causative agent. Subsequent experimental proof supports this view.

Since the use of toilet preparations containing bergamot oil is widespread, this oil is perhaps the most frequent cause of photodermatitis. The relation of the Persian lime to the fruit from which bergamot oil is expressed (Citrus aurantium Linne var. bergamia) is worth considering. The expressed oil from the cortex of the peel of these two citrus fruits contains at least one factor in common, viz., a substance capable of producing a photodynamic reaction. The "bergamot orange" is cultivated only for the production of oil and is grown chiefly in the Calabria district of Italy. It has been considered at one time or another as an orange, as a lemon and, more recently, as a lime. The fruit is not shaped like a lemon but is spherical and uniform in size. Limes have a wider distribution. A variety grown in the West Indies (Citrus medica, L. var. acida, Brandis) is cultivated on a number of the islands.

According to another source of information,[8] the Key, Mexican and West Indies limes are considered identical in type, while the Persian lime is also called Tahitian or Bearss lime and is well known in California under the latter designation. Expressed oil of limes (Mexican) and expressed oil of limes (West Indian) were obtained on the market. On being tested, both were shown to contain the photodynamic principle. At the same time, testing with oil from the cortex of the common Key lime, I was not able to produce a photodynamic reaction. In like manner I could elicit no photodynamic action using the oil from the common Valencia orange (Citrus aurantium, var. sinensis), from the lemon (Citrus medica, subspec. limona [Risso], Villa Franca, Lisbon) or from the grapefruit (Citrus paradisa).

8. Traub, H. C., and Robinson, T. R.: Improvement of Subtropical Fruit Crop, in Year Book of Agriculture, United States Department of Agriculture, 1937, p. 748.

In comparing the Tahitian, or Persian, lime with the Key lime, it is at once obvious that considerable difference exists. The Persian lime is much larger, is shaped like a lemon and, unless fully tree ripened, is a brilliant green. The peel is thicker, and the oil system in the cortex is much more highly developed. The Key lime is small and almost spherical, and the peel is thin and dry in comparison with that of the Persian lime. It has a less developed oil system in the cortex. However, lemons and oranges, as well as grapefruit, with thick peel and a large amount of oil in the cortex do not contain substances giving a photodynamic reaction.

Tests with Solar Radiation.—The first successful experimental reproduction of the dermatitis was performed by embrocation of the lime oil on my arm. The cortex of the fruit was broken by multiple pinpricks, and the oil which oozed from the rind was rubbed into the skin. The arm was subsequently exposed to the summer sun for two hours. Twenty-four hours later a slight erythema was observed. This erythema increased in depth for four days, until it had the appearance of a severe sunburn. It caused surprisingly little discomfort and only occasionally slight pruritus. During the following week there was little increase in the depth of the erythema, but gradually a brownish hue was noted, due to beginning pigmentation. This gradually increased in depth, and after about three weeks, superficial layers of the epidermis began to exfoliate. This process was complete at the end of four weeks, leaving a central bright red zone with a surrounding hyperpigmented border. As the erythema gradually faded from the center of the test area, it left a white zone of depigmentation, surrounded with a hyperpigmented border. It is still visible at the time of writing, six months later, as a slightly depigmented area, with all traces of the hyperpigmented border now absent.

This description is that of the usual evolution of the photodynamic dermatitis. It varies in degree according to the severity of the initial dermatitis. If vesiculation ensues, exfoliation and the appearance of a red central area occurs within ten days to two weeks. When the inflammatory reaction is slight, the erythema fades, leaving only a pigmented lesion, which gradually fades by an almost imperceptible exfoliation.

The depth of the reaction depends on a number of factors. Some persons are susceptible to quantitative study. With a concentrated ether extract, full strength, and with 1 to 2, 1 to 5 and 1 to 20 dilutions patch tests were made on previously unexposed skin of the abdomen. The area was exposed to the summer sun for one hour. The following reactions were read in forty-eight hours: The full strength solution elicited a 4 plus

(vesicular) reaction (fig. 2); the 1 to 2 dilution, a decided erythema (graded as 2 plus); the 1 to 5 dilution, a barely perceptible erythema, and the 1 to 20 dilution, no erythema. With the passage of time, the difference in degree of the reaction was not so noticeable, and even the 1 to 20 dilution gave rise to distinct pigmentation.

At the same time and on the same subject experiments were made to indicate the effect of time of exposure on the severity of the reaction.

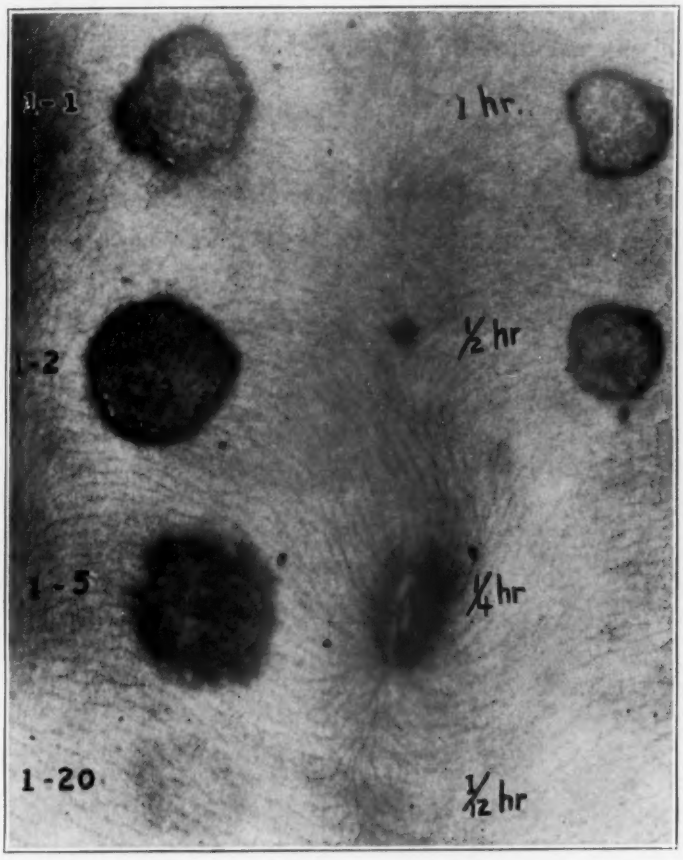

Fig. 2.—The effect of concentration of the photodynamic agent is shown at the left; the time of exposure was one hour. The effect of length of time of exposure is shown at the right.

The results are shown in figure 2. Only the slightest perceptible erythema was present from fifteen minutes' exposure, and none from five minutes' exposure.

On the same subject and at the same time ethereal, acetone, alcoholic and aqueous extractions were tested on the anterior surface of the thigh. The strongest reaction was obtained from the ether extract, the second

strongest from the acetone, the third strongest from the alcohol and the slightest reaction from the aqueous. In spite of the fact that concentrated solutions were applied, a vesicular reaction was not obtained. This area of skin had been previously exposed to the sun. The same solution applied on the abdomen of a subject known to be sensitive to the photodynamic principle produced a severe vesicular reaction. Again the ether and the acetone extracts contained a greater amount of the photodynamic substance. At a later date the same substances applied to the anterior surface of the thigh of the same subject and exposure to the sun for one hour produced a much less severe reaction.

In order to illustrate further this principle of decreased sensitivity of exposed areas, expressed oil of lime was embrocated in a streak across an area which had already been affected by the photodynamic reaction. The erythema observed at forty-eight hours was more evident in the central zone which had exfoliated and was scarcely perceptible on the normally tanned skin of the arm or in the hyperpigmented zone which surrounded the previous reaction. Pigmentation obviously affords some protection, and it was my experience that blond subjects reacted to a greater degree than brunets.

Tests with Filtered Radiation.—In order to determine the active spectral range of the rays producing the reaction, glass filters were used. In two experiments ordinary microscope slides—in one experiment two slides 0.2 cm. thick and in the other five slides 0.5 cm. thick—were used as filters. In both instances the reaction produced through the glass was almost equal in intensity to that produced by unfiltered light. Since ordinary glass is said to remove the greater part of short ultraviolet rays in the therapeutic range between 29,000 and 32,000 angstrom units, it would seem that the active spectral range, for the most part, was in the longer wavelengths. In another experiment a part of the embrocated area was covered with a circular, Wood's, filter (Corning, no. 586). This filter apparently passed the activating rays, the dermatitis produced being equal in intensity to that on the unfiltered area.

Subsequent experiments with a wider range of Corning filters were carried out in order to determine more closely the wavelength which excites the photocatalytic action. The transmission of the standard filters is represented in figure 3 by spectrophotometric curves. Experiments with these filters were carried out in the following manner: The ether extract of Persian lime oil was painted on a small area of the skin and allowed to dry. This area was covered with a 2 inch (5 cm.) square filter and was then exposed to the sun for one hour (1:00 to 2:00 p. m.). In evaluating the appearance and the result some experimental difficulties were encountered. In the first place, the filters absorbed heat from the sun, and, secondly, they prevented evaporation of moisture from the skin. This led to a collection of perspiration under the filter, and a caloric

erythema was present at the end of one hour. This tended, however, to fade before the following day, and areas which were not covered with the photodynamic agent showed little or no erythema. Figure 4 illustrates the results. The most decided reactions on the skin of the first subject tested were obtained with filters 014, 738, 586 and 395. At the same time some degree of reaction was present in each of the areas tested with filters 368 and 254. For the second subject, the strongest reactions were obtained with filters 014, 738 and 395. Only slightly less intense were the reactions with filters 586 and 385, while no perceptible erythema or subsequent pigmentation was obtained when filters 038, 368 and 254 were used.

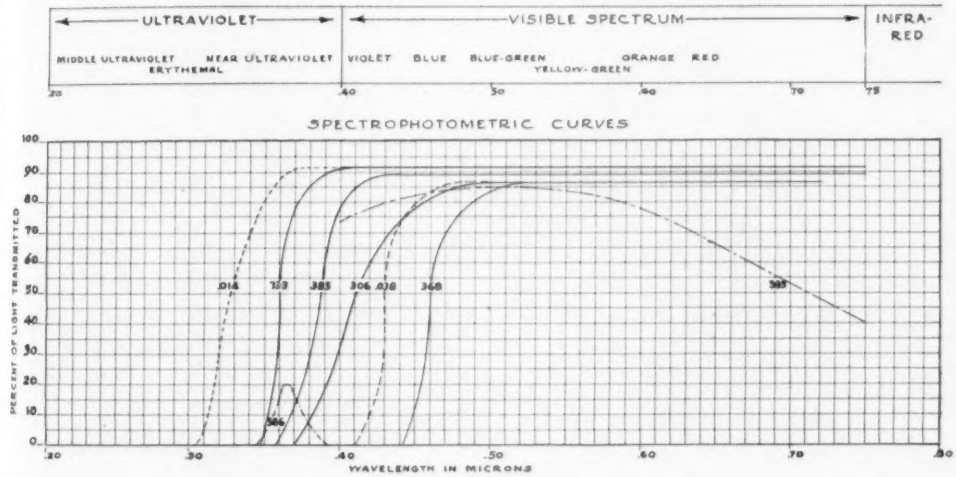

Fig. 3.—Spectrophotometric curves of the filters used, indicating the wavelength of radiation and the per cent of radiation transmitted. A spectral wavelength of 0.37 microns is the equivalent of 370 millicrons, or 3,700 angstrom units. The number on the curve indicates the Corning filter used (2 inch [5 cm.] square, polished glass and obtained from the Corning Glass Works), as follows: 014, clear blue fluorescing glass (cutoff 3,100 angstrom units); 586, violet ultra (Wood's filter) (cutoff 3,200 angstrom units); 738, H. R. nultra (cutoff 3,400 angstrom units); 385, greenish nultra (cutoff 3,600 angstrom units); 306, noviol shade 0 (cutoff 3,800 angstrom units); 038, noviol shade A (cutoff 4,100 angstrom units); 368, noviol shade B (cutoff 4,400 angstrom units); 254, heat transmitting; 395, extra light shade aklo, heat absorbing.

Referring now to the spectrophotometric curves produced by the filters (fig. 3), one sees that the active spectral range is between 3,100 and 3,700 angstrom units. Thirteen days after the tests were performed pigmentation was present in each of the areas where an erythematous response had occurred. The depth of pigmentation was roughly proportionate to the intensity of the reaction. Where vesiculation was

produced exfoliation occurred, leaving a reddened area, without the underlying pigmentation. In each test area the reaction varied only in intensity and in the amount of pigmentation produced but seemed to be identical in other respects.

The experiments as performed with the heat-resisting and the heat-transmitting filters were not satisfactory, since the glass was in contact with the skin. With filter 395, however, which transmitted both the

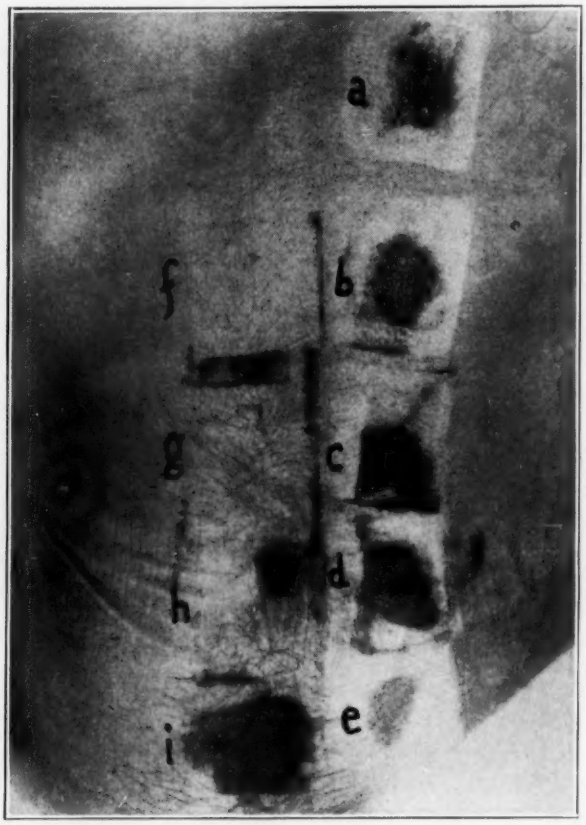

Fig. 4.—Photodynamic action of filtered radiation six days after exposure to the sun from 1:00 to 2:00 p. m.: (*a*) filter 014; (*b*) filter 586 (Wood's filter); (*c*) filter 738; (*d*) filter 385, producing strong reactions from 3,100 to 3,900 angstrom units; (*e*) filter 306; (*f*) filter 038; (*g*) filter 368; (*h*) filter 254 (heat transmitting); (*i*) filter 395 (heat absorbing). The hyperpigmentation at the edge of the experimental areas was produced by unfiltered rays. Note the erythematous reaction on the uncovered skin and its absence in areas covered by the filters. An area of intense erythema and pigmentation is produced by the photodynamic action.

visible rays and the ultraviolet rays of long wavelength, the reactions were strongly positive (fig. 4). Filter 254, transmitting no visible light

and no ultraviolet rays, caused no reaction on 1 subject and only a slight erythema on the second. While 1 of the test subjects showed slight reaction to light in the violet and blue range of the visible spectrum, a second showed no reaction from light of this wavelength. Additional experiments using infra-red radiation on embrocated areas failed to produce the photodynamic reaction. Only a slight erythema with no ensuing pigmentation was observed with this experiment.

The results with Wood's filter 586 are of interest. This filter transmits ultraviolet radiation from 3,200 to 3,800 angstrom units and passes neither short ultraviolet nor visible rays. Strong reactions were obtained in the area beneath this filter. These at first followed the usual pattern, but a delayed reaction of the urticarial type began seven days after exposure and persisted for one week.

Tests with Radiation from Artificial Sources.—As aforementioned, my initial attempts to reproduce the photodynamic reaction experimentally with an artificial source of light (quartz mercury vapor arc lamp) failed. This was because an insufficient amount of ultraviolet radiation of the longer wavelengths was present to produce the reaction. Therapeutic lamps, however, do possess some radiation in this spectral zone, and if the shorter, and particularly the erythemic, wavelengths are filtered out, it is possible to produce the photodynamic reaction.

In the following experiment a water-cooled quartz mercury vapor arc lamp was used. According to Coblentz,[9] 95 per cent of irradiated energy is less than 313 millicrons, and the greater part of this is omitted in the resonance line of mercury at 2,537 angstrom units. Nevertheless, the spectrum of this type of lamp does have an active band at 3,650 angstrom units, and all other radiation is excluded by Wood's filter (Corning 586). With a lamp with a small hand unit, the erythema time, at a distance of 1 cm., is fifteen seconds, and a distinct reaction, with subsequent peeling, is obtained from one minute's exposure. This amount of irradiation invoked no response in an area embrocated with lime oil. A similar area on the forearm embrocated with lime oil was exposed to thirty minutes' irradiation from the lamp through Wood's filter (Corning 586), which transmits long wave ultraviolet radiation at 3,650 angstrom units. Since no heat was present, no erythema was observed at the end of one-half hour's exposure. Twenty-four hours later a beginning erythematous reaction was noted. This increased in intensity throughout the week and was accompanied by eczematous vesiculation and pronounced edema and erythema. Itching was at times intense. No erythema was provoked in the areas irradiated, the reaction being confined entirely to that area which was covered with the ether extract from the Persian lime. This

9. Coblentz, W. W.: Sources of Radiation and Their Physical Characteristics, J. A. M. A. **97**:1965 (Dec. 26) 1931.

is the reaction to be expected, since the erythema-producing ultraviolet radiation was excluded. The results obtained in these experiments parallel closely those reported from the more detailed studies of Jensen and Hansen,[7] in which they used spectrographic irradiation to determine the active spectral range.

Comment.—It is well to point out that the reaction from irradiation is not the result perhaps of one particular band of radiation which excites the reaction but is rather the effect of a group of spectral waves of different lengths which harmonize or, in a physical sense, resonate in the production of the photodynamic effect.

In any event, the experiments with the filters demonstrate that ultraviolet radiation below 3,100 angstrom units exerts little or no action. Visible light likewise is relatively insignificant, the greater part having been excluded by Wood's filter, which at the same time transmits sufficient ultraviolet rays below 4,000 angstrom units to permit the photodynamic reaction. In like manner, experiments have shown that infra-red rays are not involved. They do excite a slight irritation, but it is not followed by pigmentation. Erythema due to active congestion is present immediately after exposure, and some slight eczematous reaction was obtained in some of the experiments which I conducted. No pigmentation, however, followed at the sensitized area.

NATURE OF THE PHOTODYNAMIC SUBSTANCE

The chemical nature and molecular structure of the photodynamic agent are at present unknown. The assumption that chlorophyll is the catalytic agent has been expressed by a number of investigators of these phenomena. A wide range of substances is known to excite the reaction. This subject has recently been reviewed by Sandler.[10] Many of the agents mentioned, of course, contain no chlorophyll. Furthermore, many of the agents which will produce a local photodynamic sensitization are not green; in fact, some of the best bergamot oil is brownish yellow, or honey colored.

In order to test further the theory regarding chlorophyll as a possible photocatalyzer, patch tests were performed with acetone extract of fifty plant oleoresins ordinarily used for patch tests for contact dermatitis.[11] The solutions were applied to the back of the subject in the usual manner, the oleoresins leaving bright green deposits after the acetone had evaporated. The subject was then exposed for one hour to the summer sun. She was sensitive to none of the plant oleoresins, and there was no

10. Sandler, I. L.: Photosensitizing Agents: A Brief Review of the Literature, J. A. M. A. **112**:2411 (June 10) 1939.

11. Shelmire, B.: Contact Dermatitis from Weeds: Patch Testing with Their Oleoresins, J. A. M. A. **113**:1085-1090 (Sept. 16) 1939.

photodynamic reaction. The addition of an extract containing chlorophyll from St. Augustine grass to citrus oils not possessing photodynamic activity did not alter the action of these oils on the skin.

Bergamot oil is frequently green because of a copper content. There is no question of copper contamination in my experiments in which the lime oil was applied directly from the abraded cortex of the lime peel to the skin. The fruit was first carefully washed with soap and water and rinsed, in order to remove insecticides or fertilizers which might have been deposited on the surface. The solvents used, however, ether, acetone and alcohol, were not positively known to be copper free. Goodman [12] has offered the presence of copper as an explanation for the inconsistent results obtained experimentally in photosensitization with bergamot oil. The hypothesis was advanced that the copper ion acted as a catalyzer. I have samples of bergamot oil, both yellow and green, either of which will produce the photodynamic reaction with equal intensity. The same may be said of my samples of expressed oil of lime. The materials extracted with ether, acetone and alcohol were bright green at first but have become brown after standing for three or four months. They still possess photodynamic activity.

Kuske [13] has presented experimental studies to show that the furocumarins in the parsnip possess the power to photosensitize the skin. Bergapten and oxypeucedanin, two substances in the group, had the property of rendering the skin photosensitive.

Since the chemical composition of certain of the essential oils, and particularly of the one which is the subject of my investigation, has not been investigated by methods now available, the detection of the photodynamic principle must be the subject first of further work on the chemical and physical properties of the essential oil. Attempts to reproduce the experiments with synthetic lemon and lime oils have been made, with as yet negative results. Obviously, if the photodynamic reaction could be produced with the synthetic preparation, the process of determining the offending agent would be greatly simplified.

I have observed, in the aforementioned investigations, the photodynamic reaction from oil obtained from the cortex of the lime peel and from ether, acetone, alcohol and aqueous extracts of the peel. This would tend to indicate that the photodynamic principle is present chiefly in the oily fraction of the lime peel. Experiments with juice from the lime have given uniformly negative results. The following experiment casts some doubt on this assumption. The aqueous extract used in the afore-

12. Goodman, H.: Copper as Cause of Perfume Dermatitis and as Suntan Stimulant, Arch. Dermat. & Syph. **34**:271 (Aug.) 1936.

13. Kuske, H.: Photosensitization of Skin by Furocumarins as Cause of Various Phytogenic Dermatoses: Experimental Studies, Arch. Dermat. & Syph. **38**:727-736 (Nov.) 1938.

mentioned experiment was made by extracting the cortex of the Persian lime with ordinary distilled water for forty-eight hours at room temperature. When first prepared it was greenish. No preservative was added. Fermentation ensued, and after several months the extract became brown. A portion of this aqueous extract was washed with ether in a separatory funnel, and three fractions were obtained: first, an aqueous fraction which retained the brownish color; second, an ether fraction with a slight greenish tinge, and, third, a brownish gelatinous mass (pectin?). The last-mentioned substance, which precipitated from the aqueous extract and was not soluble in ether, showed by far the strongest photodynamic activity, although reactions were still obtained with both the ether and the aqueous fractions.

SUMMARY

Oil from the Persian lime (Citrus aurantifolia, var. Swingle) is presented as a cause of photodermatitis, and 11 cases are reported in which this reaction was observed.

A photodynamic reaction was experimentally produced by embrocation of oil from the Persian lime on the skin and subsequent solar irradiation.

Experiments are presented to show that the concentration of the photodynamic agent, the length of time of exposure, the subject, the location of the application and previous irradiation determine the intensity of the subsequent dermatitis.

The longer wavelengths of ultraviolet radiation, just below the zone of visible light (3,100 to 3,700 angstrom units), are involved in the production of the dermatitis and subsequent pigmentation.

The chemical nature of the photocatalytic agent remains undetermined.

ABSTRACT OF DISCUSSION

DR. SAMUEL M. PECK, New York: There are really two phases to the reaction: vesiculation and pigmentation. The mechanism of the pigment formation is of importance, since it bears an important relation to the cause of the berlock dermatitis. As I reported many years ago (Pigmentstudien, *Schweiz. med. Wchnschr.* **59**:1227, 1929), in man hyperpigmentation of the skin can be produced by certain types of irritants without the factor of sunlight. For instance, heat is well known as a factor of this kind. Certain irritating factors, such as cantharides plaster, produce vesiculation which heals with subsequent pigmentation even in total darkness. One of the explanations for the production of berlock dermatitis is that the bergamot oil in perfume and sweat may produce a droplet which acts as a lens, thus first sensitizing the skin and then concentrating the effects of the ultraviolet rays to produce the berlock dermatitis. If the fact is borne in mind that vesiculation alone can produce hyperpigmentation, it may be a simple explanation for this phenomenon.

DR. SAMUEL W. BECKER, Chicago: I believe that Dr. Sams has initiated an important study.

Some plants contain considerable quantitites of oil. I saw one of Dr. Sams's patients who had this type of reaction after the handling of parsley, which is closely related to celery. Wild parsley has been reported as the cause of this variety of dermatitis. Botanists tell me that these plants are distinguished by the facts that there are oil ducts throughout the entire plant and that a characteristic oil is given off.

In the clinic my associates and I also tried to reproduce berlock dermatitis, but we were unsuccessful, I think, because we used irradiation from a quartz mercury vapor lamp. One evidently must use natural sunshine or some close substitute, such as radiation from a carbon arc lamp. We tried filtration experiments with the carbon arc lamp but obtained no reaction whatever, probably because the rays were not sufficiently strong. Dr. Sams is fortunate in being situated where there is ordinarily a great deal of sunshine.

The mechanism of the reaction, of course, is not known. The study of volatile oils has not been carried out to a sufficient degree to determine whether some substance in the oil is altered by the action of light and thus becomes an irritant. It will take considerable study by chemists, I believe, before the problem will be solved. However, I hope that Dr. Sams continues with this work.

Dr. Herman Sharlit, New York: This excellent presentation further confounds me in an understanding of what one expects to find in berlock dermatitis. One is impressed not so much with the dermatitis as with the discoloration of the skin. Many patients never show dermatitis but merely discoloration.

I recently had occasion to take a piece of skin from a patient suffering from berlock dermatitis and examined the specimen by frozen section. The patient had had cologne poured on his back while he was on the beach and had a general browning from the sun, but in addition he had an irregular mottling of the back and of the sides of the chest along the course of the poured cologne. The section showed distinctly that there was in the epidermis and in the cutis a deposition of foreign matter, which easily accounted for the irregularity of the discoloration seen at times from using cologne and which permitted the name berlock—necklace type—discoloration.

When radiant energy is necessary to produce the reaction, of itself it produces normal pigment, so one can expect a hyperpigmentation, a true increase of melanin. But if it is proved that this discoloration is nothing but a superimposed deposition of foreign material that is converted into a black deposit precipitated in the skin, then it might be considered that one is dealing with two elements in the formation of this type of discoloration. However, this presentation is important in giving a clue as to how to study the problem further. In some instances this foreign material may not be deposited in the skin and the stimulation of true melanin is the only end result. I am simply trying to interpret the one experience I have had with a biopsy specimen.

Dr. Bedford Shelmire, Dallas, Texas: It is a well known fact that solar dermatitis costs the stock growers of the Southwest millions of dollars annually. Sheep and white-skinned cattle are prone to have a vesicular dermatitis after the eating of certain weeds and subsequent exposure to the sun. The ingestion of the same weeds during cloudy weather is not followed by dermatitis. I am convinced that in most instances solar dermatitis in man is caused by ingestion of some particular food or drug and subsequent exposure to sunshine. I have given patch tests with acetone extracts of fruits and vegetables to many solar-sensitive patients and then exposed the tested areas to the midday sun. On 2 occasions positive reactions were obtained with the extract of parsley. All other tested sites remained normal.

Neither of the patients who gave positive reactions to parsley admitted the ingestion of this plant. I should like to suggest that Dr. Sams feed some of his patients an appreciable quantity of lime rinds and then expose them to sunshine. This procedure might prove that certain ingested foodstuffs may cause solar sensitivity in man.

DR. GEORGE M. MACKEE, New York: It is a well known fact, as Dr. Sams has pointed out, that the radiation from an ordinary therapeutic ultraviolet ray generator will not produce this peculiar reaction unless the dose is sufficient to produce exceeding discomfort. It apparently requires radiation in the visible spectrum and, as Dr. Sams said, wavelengths close to the ultraviolet, in other words, long wavelengths. I wonder why that is so. The only explanation of which I can think is that the long wavelengths are more penetrating. It was thought for many years, for instance, that ultraviolet radiation could be obscured completely by the use of glass. Some years ago Dr. Lewis demonstrated fluorescence of fungous colonies through glass. So it may be that greater penetration into the skin by the long wavelengths produces this peculiar reaction.

DR. WILEY M. SAMS, Miami, Fla.: I have considered the suggestion that Dr. Becker has offered regarding failures in the experimental reproduction of berlock dermatitis. In reading over the literature I encountered a number of ingenious theories which attempted to explain the occurrence of berlock dermatitis and the failure to reproduce it experimentally. One thing which has not been mentioned by discussers is that not all bergamot oil is the same. I have found some references to the manufacture and adulteration and to the production of synthetic bergamot oil, which I think might well explain this discrepancy. Perhaps the agent causing the photodynamic reaction is not present in all samples of bergamot oil. I believe the best way to determine the presence of the photodynamic substance is to test it directly on the skin, at least until one is more familiar with the chemistry of these essential oils and other substances which have the power of producing the photobiologic response. So far, in the experiments which I have carried out I have had no difficulty in producing the reaction if sufficient radiation from the sun is given or if the longer wavelengths from an artificial source are used, as described in the experiments on lime oil dermatitis.

I did not intend to enter the discussion on berlock dermatitis, because my paper really concerns lime dermatitis, but I believe the mechanism involved is the same, or similar.

There is at times a delayed response, which one might consider an acquired or altered reaction. I noticed in my last experiment, using filtered ultraviolet radiation from a quartz mercury vapor glow lamp, that after a number of such experiments had been made, there was a delayed urticarial reaction. This occurred approximately one week after the initial response and was similar morphologically to the urticaria sometimes seen as a result of exposure to sunlight. It itches intensely and lasts approximately a week. I did not observe this on my other subjects, but I was able to repeat it on my arm in the experiment cited, using the quartz mercury vapor glow lamp.

Dr. Becker and I went through a course in taxonomy, and we tried to get some exact information on the botanic relation of the various limes and the differences between seedlings and those produced by grafting in various parts of the country. We found a number of things of interest pertaining to limes and their relation to the bergamot orange.

The question of discoloration was raised, and I discussed this point with Dr. Becker, knowing his interest in the field of pigment production. I feel that this

condition is a melanosis. It follows a course much like sunburn, except that the intensity is greater. It is well known that where sunburn is intense enough to produce vesiculation and desquamation of the skin little pigmentation will remain. This is the effect which Florida visitors try to avoid. They want to get as deep a tan as possible, but they do not want to peel. I have always considered that the pigmentation produced by the sun was the result of melanin formation and I believe the pigmentation which follows the photodynamic reaction is similar.

The reason berlock dermatitis is seen only as a pigmentation is, I think, a matter of degree. One of my patients, a physician's wife, had a reaction so severe from eau de cologue that it was necessary to give her an opiate in order to control the pain. She had an exceedingly extensive bullous reaction, accompanied by urticaria and edema, and of course this was followed by desquamation. The involved area was red throughout the center and hyperpigmented at the border when the reaction subsided. In many cases the patient does not notice the erythema because it is slight. There is not much pruritus, and the first thing noticed is the pigmentation. Treatment is applied for because the patient does not like the appearance of the streak on the neck or throat.

I do not know just how to approach the problem of feeding patients photodynamic substances in order to produce a systemic response. There is some work being carried on in experimental animals, feeding them buckwheat until they become light sensitive. The Kettering Foundation at Antioch College in Yellow Springs, Ohio, is doing investigative work on the nature of chlorophyll. As a sideline they have been studying the photodynamic action produced in white rats by feeding. My studies have been concerned entirely with the cutaneous reaction. I am not sure that feeding experiments with some of the photodynamic agents are safe for clinical investigation. I recall one report in the literature of a man who took one of the porphyrins and was sensitive to sunlight for approximately two years thereafter.

ARGYRIA

WITH SPECIAL REFERENCE TO THE CUTANEOUS HISTOPATHOLOGY

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AND
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ROCHESTER, MINN.

The subject of argyria has been reviewed in a recent monograph by one of us (W. R. H.) and Pillsbury.[1] We wish to present briefly the clinical data of 68 additional cases of generalized argyria observed at the Mayo Clinic. In 17 of the cases, specimens of skin were removed for biopsy. We wish to emphasize the importance of histologic study in confirming the diagnosis of argyria and in differentiating argyria from other cutaneous pigmentations, especially those due to other heavy metals.

CLINICAL DATA

In the twenty-five years from 1915 to 1939 inclusive, 68 persons who had generalized argyria were seen at the Mayo Clinic, 41 of whom came after 1930. Females were more numerous than males in this series, in a ratio of 7:4. At the time of the first examination the youngest person was 6 years of age and the oldest 78. Two thirds, or 44, of the persons were in the age groups from 40 to 60 years. Six patients were physicians. The clinical appearance of the pigmentation as noted by the patient or relatives varied from six months to fifteen years after the initial use of silver, the pigmentation appearing first, in the majority of cases, after the silver had been employed constantly or intermittently for two to three years. The length of time that our patients used silver varied from a few months to twenty-five years, with the peak at two to three years. Inquiry as to the reason for using silver disclosed that 50 per cent had employed it for various gastrointestinal disturbances, 33 per cent for diseases of the upper part of the respiratory tract and 17 per cent because of pathologic conditions of the vagina and urethra.

Two thirds, or 44, of the persons had taken silver compounds in the form of pills or capsules by mouth or as drops, paint or sprays in the

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From the Section on Dermatology and Syphilology of the Mayo Clinic.

1. Hill, W. R., and Pillsbury, D. M.: Argyria: The Pharmacology of Silver, Baltimore, Williams & Wilkins Company, 1939.

nose and throat. The remaining third irrigated with silver preparations or instilled them into bodily orifices. Forty-five persons were able to supply the name of the silver compound used. Silver nitrate was the only salt used by 22, mild protein silver (argyrol) by 10 and neo-silvol by 5 persons. Eight patients had employed combinations of silver salts or less well known colloidal silver preparations. The data on dosage in this series are insufficient. The reader may consult the monograph by Hill and Pillsbury regarding this point. It is of interest to note that 2 of our patients gave a history of concomitant ingestion of a bismuth compound. We suspect that other persons in the group who had used silver for gastrointestinal disturbance had also taken a bismuth preparation.

HISTOLOGIC STUDY

Specimens of skin which had been removed for biopsy were studied by direct and by dark field illumination. Stained and unstained sections were examined.[2]

All authors who have studied by direct illumination microscopic sections of skin from persons who had generalized argyria agree that silver is deposited exclusively in the cutis and never in the epidermis or its appendages.[3] Unna,[4] in 1896, stated that "the deposit of silver is always limited exactly to the margin of the connective tissue and especially affects the elastic fibers and firm bounding membranes, avoiding altogether the protoplasmic parts of the connective tissue and the epithelium with its appendages." In the writings of Frommann,[5] Riemer [6] and Neumann [7] attention is called to the constant presence of a well defined streak or band at the subepithelial margins, the so-called subdermal line. Granules of silver were seen in the papillary bodies.[8] Gans [3a] noted that small, fine round brownish black granules were deposited on the membrana propria of the sweat glands and on the connective tissue membrane about the sebaceous glands and hair follicles.

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2. Habermann, R.: Ueber Argyria cutis nach Silbersalvarsan und den Wert der Leuchtbildmethode E. Hoffmanns für ihren Nachweis, Dermat. Ztschr. **40**: 65-80, 1923.

3. (*a*) Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2, pp. 152-155. (*b*) Kanitz, H.: Ueber Argyrie der Haut, Arch. f. Dermat. u. Syph. **94**:49-70, 1909.

4. Unna, P. G.: The Histopathology of the Diseases of the Skin, translated by N. Walker and P. G. Unna, New York, Macmillan & Company, 1896, p. 1190.

5. Frommann, C.: Ein Fall von Argyria mit Silberabscheidungen im Darm, Leber, Nieren und Milz, Virchows Arch. f. path. Anat. **17**:135-147, 1859.

6. Riemer, B.: Ein Fall von Argyria, Arch. d. Heilk. **16**:296 and 385, 1875; **17**:330, 1876.

7. Neumann, I.: Ueber Argyria; Teinte bronzée s. ardoisée de la peau; Bleifarbe der Haut, Med. Jahrb., 1877, pp. 369-384.

8. Stillians, A. W.: Argyria, Arch. Dermat. & Syph. **35**:67-77 (Jan.) 1937.

Similar granules have been described in the walls of arteries, capillaries and veins, in smooth muscle, sarcolemma and neurilemma [9] and also in the subcutaneous tissue.

In sections stained with hematoxylin and eosin, but more clearly in sections stained lightly with polychrome methylene blue, under the low power objective the sweat and sebaceous glands appear to be outlined by a brownish line and a similar line exists at the junction of the epidermis and the cutis. With higher magnification one sees that these lines are composed of numerous discrete granules in the membrana propria of the sweat glands and also in connective tissue sheaths about the sebaceous glands and hair follicles. In the papillary bodies the granules seem to form intertwining and interlacing chains resembling chains of streptococci. Individual brown to black granules also are scattered profusely throughout the cutis without relation to the underlying structure. Granules of silver also can be seen in the intima and in the adventitia of the larger arteries and to a less extent in the walls of the smaller blood vessels. The arrectores pilorum muscles and bundles of cutaneous nerves also appear infiltrated. The granules vary slightly in size and shape but are for the most part round. They are about a tenth the diameter of an erythrocyte,[10] although some may be smaller. Occasionally the granules are matted together in larger clumps. In our sections the epidermis was entirely free of any silver particles. The cells of the sebaceous and sweat glands did not contain granules of silver. Elastic tissue stains revealed predilection of granules of silver for elastic fibers, in which they seemed to be embedded.

Granules of silver are always to be demonstrated in the membrana propria of the sweat glands, and usually large numbers of granules form a line just beneath the epidermis. In half of the cases, granules could be observed in the middle and deep portions of the cutis, as well as in the connective tissue membrane about the sebaceous glands and hair follicles.

The dark field method of illumination first introduced by Eric Hoffmann was employed in the study of argyria by his pupil Habermann.[2] The latter obtained the best results by using a paraboloid condenser with interchangeable direct and dark field condensers, permitting direct comparison of the same part of the slide. In our studies we simply used a dark field microscope, such as is set up for study of spirochetes in syphilis, and marked areas when necessary for comparison with direct illumination. It is best to study sections stained

9. Habermann.[2] Kanitz.[3b] Neumann.[7]

10. Spiegel, L.: A Discoloration of the Skin and Mucous Membranes Resembling Argyria, Following the Use of Bismuth and Silver Arsphenamine: Report of Three Cases with Microscopic Examination, Including Spectrographic and Chemical Analyses of the Tissues, Arch. Dermat. & Syph. **23**:266-286 (Feb.) 1931.

lightly with polychrome methylene blue, although refractile granules of silver may be demonstrated easily even in sections stained routinely with hematoxylin and eosin.

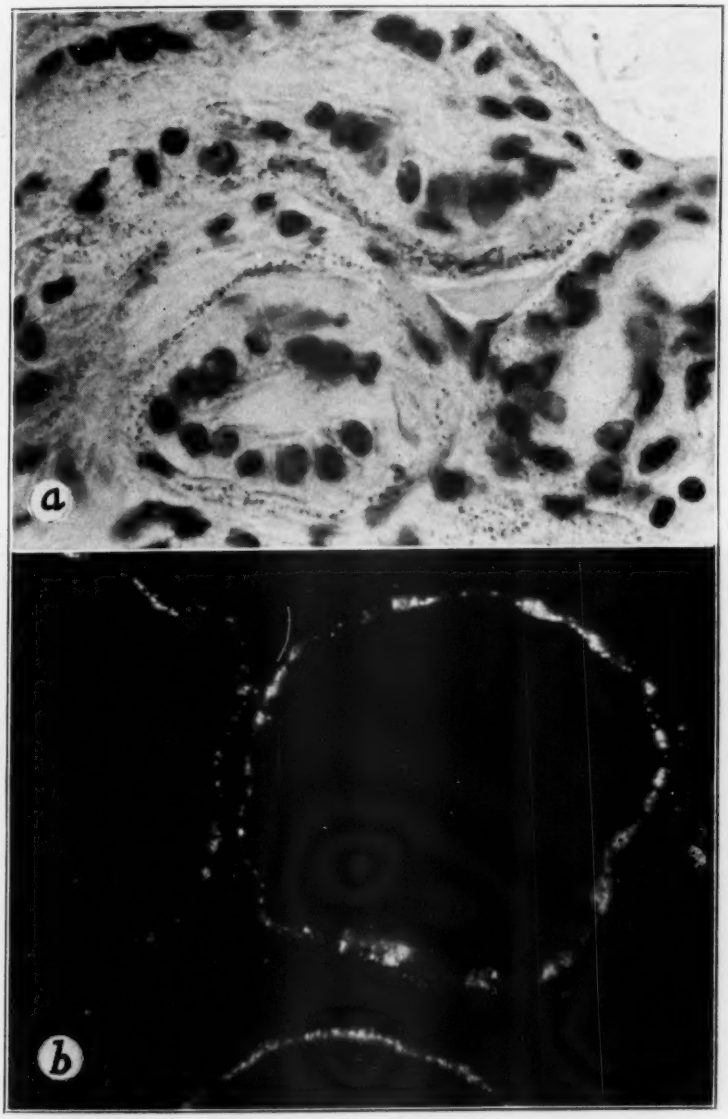

Fig. 1.—Granules of silver. *a*, in the membrana propria of the sweat glands (hematoxylin and eosin stain, × 700). *b*, apparent variation in size results because not all the granules are in the same focal plane (dark field, × 750).

The dark field method is of distinct value in cases of argyria because it gives better definition to the granules of silver than direct illumination

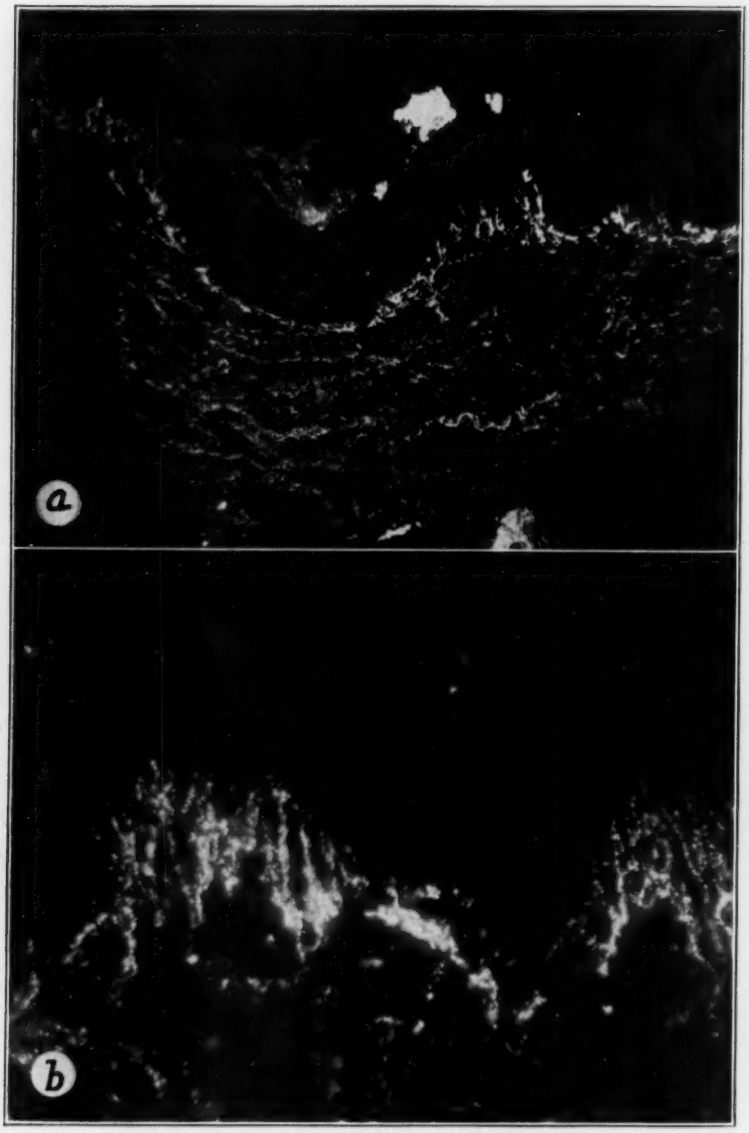

Fig. 2.—Granules of silver (*a*) throughout the cutis and condensed into so-called subepithelial line (subdermal line) in the papillary region (dark field, × 160) and (*b*) arranged in cocci-like chains in the papillary bodies (dark field, × 380).

does and also brings into view many granules which are not evident with direct light.[11] With a low power objective the circumferences of the sweat glands are illuminated brilliantly by yellowish white lines

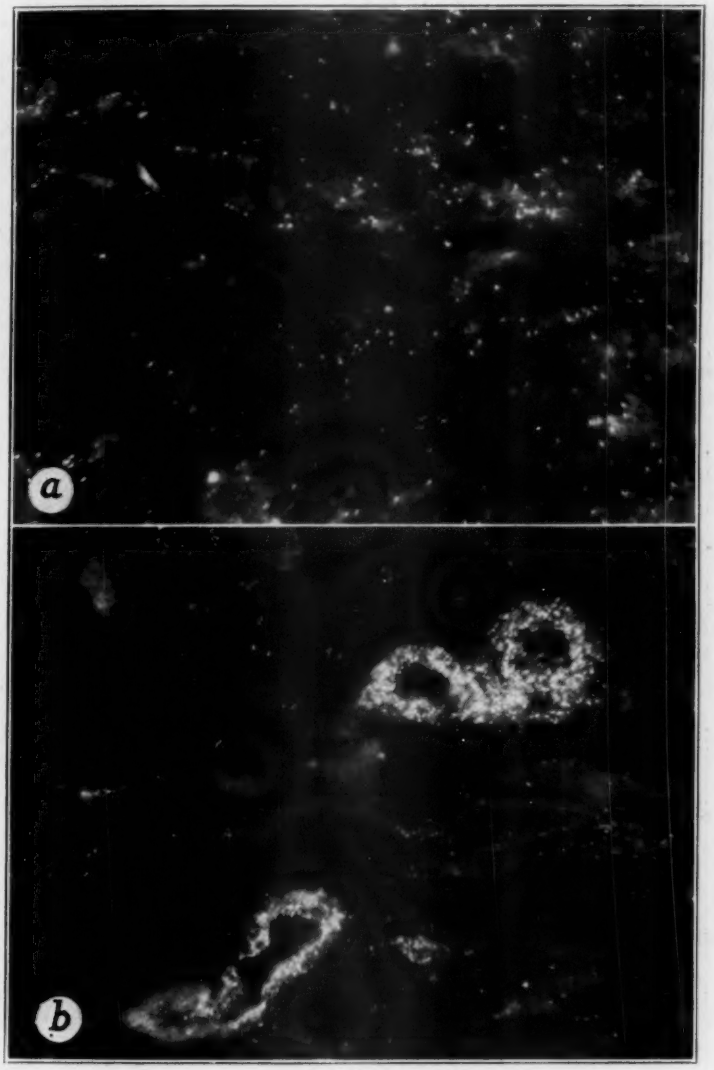

Fig. 3.—Granules of silver scattered diffusely (*a*) throughout the cutis (dark field, × 540) and (*b*) in the vessel wall in the midcutis (dark field, × 375).

against a dark background. Higher magnification reveals brilliantly refractile golden white granules, which appear much more numerous

11. Zoon, J. J.: Ueber histologische Befunde bei Argyria cutis, Dermat. Ztschr. **70**:125-133 (Nov.) 1934.

than they do with direct illumination (fig. 1). The granules of silver are deposited in the membrana propria but not in the cells of the sweat and sebaceous glands. The distribution of the granules appears the same on dark field examination as under direct illumination (figs. 2, 3

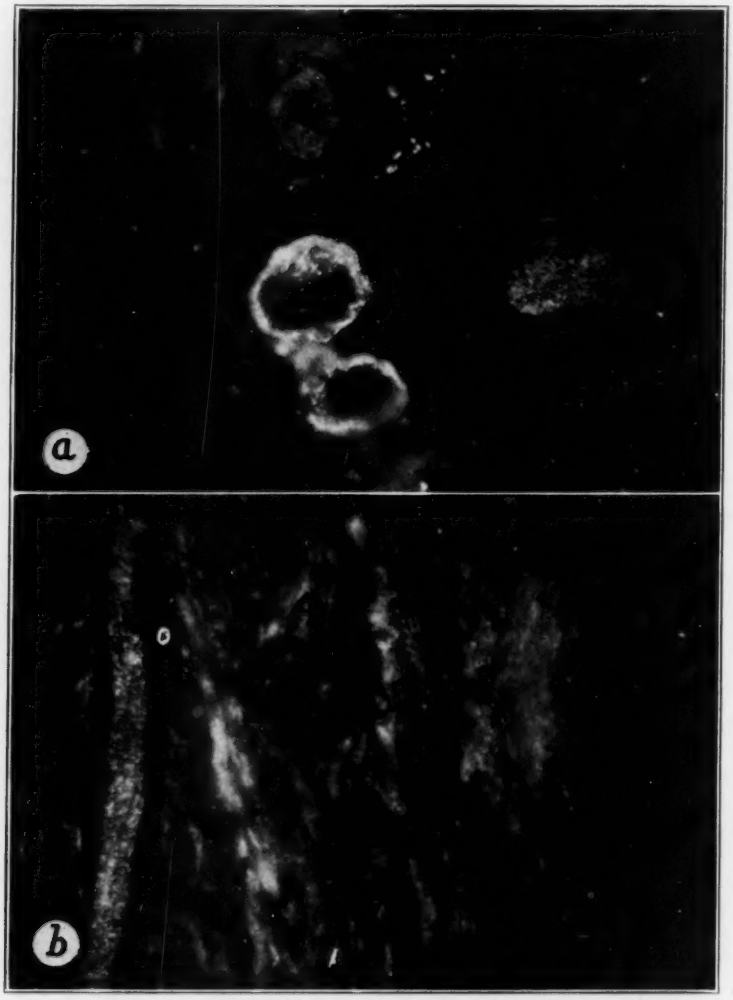

Fig. 4.—*a*, the membrana propria of the sweat glands laden with granules of silver and, at the right, cutaneous nerve bundles containing granules of silver (dark field, × 280). *b*, the arrector pili muscle at the left is outlined by refractile particles of silver; a hair follicle is seen at the right (dark field, × 250).

and 4). The so-called subdermal or really subepithelial line is most prominent, and also the arrangement of the granules in chains like cocci. Discrete granules of silver are also seen scattered throughout the connective tissue and have been referred to as "stars in the heavens."

Again it was apparent with special stains that marked deposition of granules of silver occurred in the elastic fibers. One cannot draw any conclusions regarding deposition of silver in the reticulum, or *Gitterfasern,* as staining with solutions of silver is necessary to demonstrate these fibers. With the dark field illumination, granules of silver are demonstrable in the interlobar tissue of the subcutaneous fat, in the hair follicle and even in the hair shaft.

COMMENT

We are in accord with Habermann [2] and Zoon [11] that intracellular deposition of granules of silver occurs in the endothelial cells, fibroblasts and mast cells. The mast cells were increased in number in many of our sections. One must agree, however, with Lenartowicz and Jalowy [12] that with present available methods one cannot be sure whether or not silver is found intracellularly. These authors assumed that initial deposits of silver occur in the reticuloendothelial system with extracellular deposits later.

We have mentioned the apparent affinity of silver for elastic fibers or the selective binding of the silver by the elastic fibers. Granules of silver are seen in the same subdermal location and in the same area as that in which elastic fibers occur in sections of normal skin, as has been reported by Ejiri [13] and by us.[14] In other words, the silver in the form of a subepithelial line and the finger-like chains of granules of silver projecting into the papillary bodies probably are simply elastic fibers which have bound the silver, although possibly granules of silver are deposited in the *Gitterfasern* (reticulum fibers).

Deposition of silver apparently, however, has no pathologic effect on the elastic fibers, which stain in a normal way and appear unaltered under ordinary direct illumination. In fact, deposition of silver either in skin or in internal organs causes no appreciable pathologic changes. There is no inflammatory reaction in the skin. Some increase in the tissue mast cells apparently occurs, and in many cases there is an increase

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12. Lenartowicz, J., and Jalowy, B.: Essais de production d'argyrie artificielle chez les animaux, Ann. de dermat. et syph. **9**:483-494 (June) 1938.

13. Ejiri, I.: Studien über die Histologie der menschlichen Haut. I. Mitteilung: Ueber den regionären Unterschied der elastischen Fasern der Haut, Jap. J. Dermat. & Urol. **40**:173-174 (Nov. 20) 1936; II. Mitteilung: Ueber die Alters- und Geschlechtsverschiedenheiten der elastischen Fasern der Haut, ibid. **40**:216-217 (Dec. 20) 1936; III. Mitteilung: Ueber die regionären- und Altersunterschiede der verschiedenen Hautelemente mit besonderer Berücksichtigung der Altersveränderung der elastischen Fasern, ibid. **41**:8-12 (Jan. 20), 1937; IV. Mitteilung: Ueber das Wesen der Altersveränderung der Haut, ibid. **41**:64-70 (Feb. 20) 1937.

14. Hill, W. R., and Montgomery, H.: Regional Changes and Changes Caused by Age in the Normal Skin: Histologic Study, J. Invest. Dermat. **3**:231-245 (June) 1940.

in melanin in the basal cells in the epidermis, together with increase in the number of chromatophores laden with melanin in the upper part of the cutis. We have emphasized that there is no deposition of silver in the epidermis and that therefore there is no dermal-epidermal[15] exchange of granules of silver, such as apparently occurs in the deposition of hemosiderin in hemochromatosis and is seen in pigmentation due to arsenic, bismuth, gold and mercury. Any metallic deposit in the skin would seem to stimulate melanoblastic cells to increase the formation of pigment, but in the case of silver one must presuppose that this increase in melanin pigment results from close proximity of the granules of silver in the subepithelial line rather than from direct contact with the basal and other melanoblastic cells in the epidermis.

There was no appreciable variation in the number, size or location of the granules of silver in the specimens of skin removed for biopsy in any of our cases, in spite of the fact that the patients undoubtedly took and absorbed varying quantities of silver. All our specimens for biopsy were taken from the pigmented skin. One patient, however, had a nevus removed from the nonpigmented skin of the leg, and in the normal skin adjacent to the nevus there were granules similar in size, shape, number and location to those in sections from the pigmented skin. Habermann stated that microscopically the silver content was the same in two different specimens of skin taken for biopsy from the same patient, the first specimen from the pigmented skin of the face and the second from the nonpigmented skin of the abdomen. This tends to support the results of Gaul and Staud,[16] who stated:

> The pathologic changes in argyria as well as the histochemical studies have demonstrated a uniform distribution of the silver throughout connective tissue. Since the corium of the skin is of mesodermic origin or connective tissue, the biopsy specimen will contain the same quantity of silver in the same patient irrespective of the site from which it is obtained; i. e., a biopsy specimen obtained from the area of discoloration and one obtained from the leg or thigh showing no discoloration will contain equal quantities of silver in the same patient.

DIFFERENTIAL DIAGNOSIS

The bluish gray or slate-colored skin of most patients who have local or generalized argyria is in itself diagnostic. When, however, there is increase in melanin pigmentation, the increase in melanin may mask

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15. Pautrier, L. M.: Dermo-Epidermic Interchanges as Controlled by the Study of Melanic Pigment, the Esters of Cholesterol (Xanthoma) and Hemosiderin (Schamberg's Disease), Arch. Dermat. & Syph. **17**:1-15 (Jan.) 1928.

16. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: Seventy Cases of Generalized Argyrosis Following Organic and Colloidal Silver Medication, Including a Biospectrometric Analysis of Ten Cases, J. A. M. A. **104**:1387-1390 (April 20) 1935.

the grayish color or result in a brownish hue or a bronzing of the skin simulating the appearance of hemochromatosis. Pigmentation from mercury also gives a bluish gray pigmentation, but in localized forms from the use of cold creams it is distinguished readily by accentuation of pigmentation in the folds of the skin.[17] In cases of argyria there often is a question of additional pigmentation resulting from ingestion of bismuth. Clinically, pigmentation due to arsenic is distinguished easily from argyria. That due to gold or bismuth may not be differentiated so easily.

Histologic differentiation of argyria [18] from other kinds of pigmentation is made readily, especially when dark field illumination is employed. In Addison's disease and arsenical pigmentation there is an increase in melanin pigment and granules of melanin are not refractile under dark field illumination. In hemochromatosis stains for hemosiderin reveal deposits of hemosiderin occurring as large irregularly clumped granules in relation to the membrana propria of the sweat glands and also outlining the reticuloendothelial system of the skin and even occurring in basal and dendritic cells in the epidermis. The granules of silver are much smaller and more uniform in size than those of hemosiderin, and, as Spiegel [10] has emphasized, the hemosiderin is nonrefractile with dark field illumination.

In pigmentation due to mercury, whether from the use of cold creams or in tattoo marks, the mercury is deposited in large coarse granules and clumps throughout the epidermis and cutis without any special affinity for the membrana propria of the sweat glands. The refractility of particles of mercury is less than that of the granules of silver except when the particles of mercury are in larger clumps.

Two of our patients had taken a bismuth preparation as well as silver. There was no difference in the pigmentation in the skin on examination by either the direct or the dark field method. Spiegel reported a similar experience. He was unable to differentiate one pigment from the other by either method of examination, although spectroscopic examination of the biopsy specimen showed that both metals were present. His microscopic findings were what we considered would be characteristic of silver. Leuth, Sutton, McMullen and Muehlberger [19] reported a case of generalized pigmentation due to bismuth,

17. Goeckerman, W. H.: A Peculiar Discoloration of the Skin: Supplementary Report, J. A. M. A. **84**:506-507 (Feb. 14) 1925.

18. Montgomery, H., and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans and Hemochromatosis, Arch. Dermat. & Syph. **21**:970-984 (June) 1930.

19. Leuth, H. C.; Sutton, D. C.; McMullen, C. J., and Muehlberger, C. W.: Generalized Discoloration of the Skin Resembling Argyria Following Prolonged Oral Use of Bismuth: A Case of "Bismuthia," Arch. Int. Med. **57**:1115-1124 (June) 1936.

and Wiener [20] reported a case of localized bismuth pigmentation. In both cases the pigment was deposited near the epidermis in the papillary bodies and in the cutis, but no mention was made of deposition in the membrana propria of the sweat glands. It would seem that deposition of bismuth more nearly parallels that of mercury in instances of pigmentation due to mercury.

Cascos,[21] who has studied several cases of gold pigmentation, reported that he was able to distinguish granules of gold precipitate in the skin from granules of silver on dark field examination. He claimed that the granules of gold are larger and more irregular than those of silver. He also wrote that gold has a "different location, that it is usually in the interior of macrophages or in the neighborhood of blood vessels but may also be found in the same location as silver but in smaller amount." He stated that granules of silver take the form of uniform crystals but that gold seldom does.

Kochs [22] described refractible particles of metallic gold under dark field illumination deposited chiefly in the upper layers of the corium and also in the basal cell layer. With direct illumination, large irregular masses or clumps of the material are shown on the photomicrograph, again simulating the histologic picture of bismuth pigmentation more than that of silver pigmentation.

SUMMARY AND CONCLUSIONS

The clinical study of 68 additional cases of generalized argyria confirms the previous observation of one of us (W. R. H.) and Pillsbury that the incidence of argyria is increasing. According to our clinical data, the average person who has generalized argyria is a woman, 40 to 60 years of age, who has used silver nitrate, mild protein silver (argyrol) or neo-silvol for gastrointestinal disturbance or disease of the upper part of the respiratory tract constantly or intermittently for two to three years and whose skin was observed to change color in the two to three years, as an average, after she began to use the silver salts.

Our biopsy studies by direct illumination and dark field methods of examination disclose that silver is not deposited in the epidermis but is seen in relation to the elastic fibers in the cutis, to the membrana propria of the sweat glands, to the connective tissue sheaths about the sebaceous glands and hair follicles and to the cutaneous vessels, muscles

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20. Wiener, K.: Vaginal Melanosis Caused by Bismuth Therapy and Carcinoma of the Cervix, Arch. Dermat. & Syph. **42**:23-29 (July) 1940.

21. Cascos, A.: Étude comparative des pigmentations métalliques. Argyrose et chrysose, Ann. de dermat. et syph. **7**:751-762 (Aug.) 1936.

22. Kochs, A. G.: Zur Kenntnis der Chrysiasis, Arch. f. Dermat. u. Syph. **178**: 323-330, 1938.

and nerves. Granules of silver are seen most frequently about the sweat glands and in the papillary bodies at the so-called subdermal or subepithelial line.

Recognition of granules of silver under dark field illumination is so easy that this method is the one of choice in microscopic study of specimens removed for biopsy from the skin of persons who have generalized argyria.

Our studies give evidence that silver is deposited intracellularly and that it is bound by normal elastic fibers. Silver pigment causes no pathologic change in the skin. The number, size and location of the granules of silver observed microscopically in the specimens of skin removed for biopsy from persons who have generalized argyria do not depend on the amount of the silver used or on the site from which the specimen is taken.

For microscopic diagnosis a specimen can be taken for biopsy from the nonpigmented skin of persons who have generalized argyria. In some cases silver causes an increased production of melanin.

The skin of persons who have generalized argyria presents a characteristic and easily recognizable microscopic picture and can be differentiated from the skin of persons who have Addison's disease, hemochromatosis, pigmentation due to arsenic or local pigmentation due to mercury or, according to reports from the literature, to gold. The location and character of deposits of bismuth in bismuth pigmentation also differ from those seen in argyria. When the two metals are present at the same time, spectrophotometric studies may be indicated.

CORAL DERMATITIS

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AND
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This report is the first in the literature of a case of dermatitis caused by a stinging coral animal.

The majority of corals belong to the class of flower animals, or Anthozoa, and this article is confined to a dermatitis contracted from one of these animals. A coral polyp, or sea anemone, is a cylindric animal of lowly organization, with a mouth surrounded by tentacles at the top of the cylinder and with but one main cavity (the coelenteron) inside. It has stinging cells on its tentacles with which it can paralyze its prey.

Dana [1] described the properties of the Actinia genus of polyps, which have what Agassiz called lasso or nettling cells. These tubular cells escape from the chief cell by turning themselves inside out, the harpoon-like extremity showing itself last with lightning-like rapidity. The lasso cells are usually less than $\frac{1}{200}$ inch (0.13 mm.) in length and are thickly crowded in the larger part of the skin or walls of the tentacles, about the mouth and walls of the stomach and within the visceral cavity. They appear as white cords which hang in folds from the edge of the septums. A mollusk or crab falling on this flower is at once poisoned by the minute lassos and is rendered incapable of resistance.

While Actineae have no internal coral secretions, they form a thickened epidermic plate at the base and also, in a few cases, around a part of the body. This plate arises from an exudation of mucus from the surface and the entangling therein of minute particles of foreign or dead matter.

A lasso cell once used is worthless, since the tube cannot be returned to the sheath. But it is replaced by others; the supply is indefinite. Dana repeated experiments showing that the tubular thread of the lasso cell can actually penetrate the tissues of even higher animals. In some cases death ensued even to vertebrate animals from momentary contact with the capsuliferous organs of these Zoophyta.

There have been reports of peculiarly indolent lesions following cuts of the skin from coral. Byrne [2] stated that generally a coral cut

1. Dana, J. D.: Corals and Coral Islands, New York, Dodd & Mead, 1872, pp. 20 and 35.

2. Byrne, K.: Coral Cut, M. J. Australia **2**:649-650 (Dec. 20) 1924.

is slow to heal, partly owing to the fact that the sea-faring men who suffer from them wade through the surf on the beaches and do not give the cuts a chance to heal. He stated the belief that under more hygienic conditions a coral cut does not lead to a chronic lesion and that the lesion does not last longer than two or three weeks. Byrne, who sustained coral cuts, described the wounds as being 5 cm. square and of a septic character. The inflammatory reaction did not extend deeper than the subcutaneous tissue or farther than 6 mm. from the edges of any wound. During a fortnight's sepsis he felt ill out of all proportion to the area involved. The illness was more severe when compared with the general malaise usually experienced with severe cellulitis from other causes. The bacteriologic condition of the wounds was not studied. With neglect, a wound of this kind becomes a suppurative lesion.

Paradice [3] observed coral cuts sustained in the Great Barrier Reef (Australia). A mere scratch, if ignored for a few days, developed into an ulcer with a yellow sloughing base and red surrounding skin, which took a much longer time to heal than other lesions of similar size. If a coral scratch was washed with saline solution and painted with tincture of iodine at once, an ulcer did not develop, but usually a tender red indurated area around the scratch persisted for a week or more.

Castellino [4] described the lesions sustained in the coral industry as it was carried on around the Mediterranean Sea. It was his belief that they were caused not by the phenomenon of sensitization but by a particular kind of mechanical work. However, the lesions were of sufficient importance to modify the habitual line of work of the employee or even to lead to abandonment of that employment altogether. Castellino illustrated several of the lesions occurring on the palms of these workers.

These reports merely prove that coral has an unusual effect on the skin. The condition in the following case, however, is illustrative of a cutaneous lesion which developed after direct contact and not from a coral cut.

REPORT OF A CASE

J. M. S., a dentist aged 43, was first treated in September 1939 for an itching lesion of the right forearm. The patient collected coral as a hobby and habitually spent several months during the summer in deep sea diving for new specimens.

In July 1939 the patient was diving for coral near a small reef in the West Indies. As he picked up a different type of coral, he experienced a distinct stinging pain on the inner surface of the forearm. He rose to the surface and was lifted into the boat. Within five minutes he noticed that a clear fluid was oozing from

3. Paradice, W. E. J.: Injuries and Lesions Caused by the Bites of Animals and Insects, M. J. Australia **2**:650-652 (Dec. 20) 1924.

4. Castellino, P. G.: Dermatosi professionali; le alterazioni cutanee dei lavoratori del corallo, Folia med. **23**:132-140 (Feb. 15) 1937.

the affected skin. Watery beads continued to form for at least thirty minutes. After that the skin became red, edematous and itchy. Within twenty-four hours the involved area sloughed out to form an ulcer almost 2 inches (5 cm.) in diameter. Healing proceeded slowly, and several months elapsed before the ulcer was covered by a thick scar.

When the patient was first examined, in September 1939, the lesion consisted of a serpiginous band about 1 inch (2.5 cm.) in length and ½ inch (1.3 cm.) in width. This band was composed of flat and conical, variously shaped, reddish purple papules and areas of keloidal thickening. The linear arrangement of the

A, A linear band composed of flat and conical papules together with keloidal thickening of the skin. *B*, specimen of coral (Madapora palmata) which produced the dermatitis.

band as well as of the violaceous papular lesions was vaguely suggestive of lichen planus, but the conical, almost cup-shaped, papules, the keloidal scars, the absence of lesions elsewhere and the history were conclusive.

The lesion was extremely pruritic, and the patient was treated with bland lotions and roentgen radiation. After a total dose of 400 r, the pruritus subsided and the lesion disappeared, leaving a faint brownish pigmentation.

The patient made the observation that this same type of coral (Madapora palmata) does not produce a lesion when broken off by the hand.

Evidently, the epidermis of the palm is too thick for penetration by the minute stinging cell. The lesions usually appear on the leg or on the flexor aspect of the forearm.

SUMMARY

This report calls attention to the occurrence of dermatitis caused by a stinging coral animal. The eruption was primary and differed from other types of dermatitis produced by coral in that it was not preceded by a break in the skin. Immediately after the sting the affected skin showed intense serous exudation, and within twenty-four hours a sloughing ulcer appeared. Healing was slow, with keloidal formation and persistent pruritus. This was relieved by filtered roentgen ray therapy.

2 East Fifty-Fourth Street.

DERMATITIS VENENATA DUE TO NAIL LACQUER

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Dermatitis due to nail lacquer is being reported in the literature with increasing frequency. In our experience it is not a rarity but a common occurrence, especially during the past three years. Our first case was observed in 1926, and to date we have observed well over 100 examples of this condition. Because of its increased frequency and the relation to dermatitis caused by other widely used objects which are covered with lacquer, it is felt that an account of our experiences should be of value in tracing the obscure cause of this dermatitis.

In 1925 Miller and Taussig [1] reported the case of a patient with dermatitis of the neck due to nail polish. In 1937 Sulzberger [2] recorded a case of dermatitis of the eyelids, the chin, the face and the skin around the finger nails, in which a patch test with nail lacquer elicited a positive reaction. Feiler [3] reported 1 case in 1940 and Hollander [4] 3 cases. In the latter group, the eyelids were involved in each instance, and also the chin in 1, as well as the left side of the neck along the hair line and in the nuchal area. Patch tests in Hollander's cases gave negative results. Diagnosis was made by observing that elimination of the suspected substance was followed by disappearance of the eruption. Burgess [5] in 1940 reported 10 cases of dermatitis due to nail lacquer.

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Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 9, 1941.

1. Miller, H. E., and Taussig, L. R.: Cosmetics, J. A. M. A. **84**:1999 (June 27) 1925.

2. Sulzberger, M. B.: Hypersensitivity to Nail Polish, Arch. Dermat. & Syph. **36**:460 (Aug.) 1937.

3. Feiler, H. B.: Eczema Venenatum Due to Lipstick and Nail Polish, Arch. Dermat. & Syph. **42**:224 (July) 1940.

4. Hollander, L.: Nail Lacquer Dermatitis, J. A. M. A. **115**:1714 (Nov. 16) 1940.

5. Burgess, J. F.: Nail Polish Dermatitis, Canad. M. A. J. **43**:544 (Dec.) 1940.

In all but 1 the eruption was confined to the face, neck and shoulders. In all there was involvement of the eyelids, and in 1 a generalized pruritus with pruritus ani. Patch tests elicited positive reactions in all 10 cases, and the eruption disappeared promptly after the application of nail lacquer was discontinued. Recently Ellis and Kirby-Smith [6] reported 5 cases. These authors stated that there is "necessity for considering nail polish as a cause of dermatitis on the eyelids, face, neck and arms." They concluded that dermatitis due to nail lacquer can be attributed to the pure cellulose nitrate and/or to the dye. In addition to these cases of dermatitis, Greenbaum [7] reported a case of leukoplakia of the tongue, presumably due to nail lacquer scraped off with the teeth.

Before the clinical aspects of dermatitis due to nail lacquer are discussed, it is well to consider briefly the chemical composition of this substance. It first appeared on the market in 1919 [8] and was little more than a solution of collodion, which on drying left a brittle, shiny film on the nails. Since that time the composition has changed rapidly until at present it is a highly complex mixture.[9] All nail lacquers have cellulose nitrate, or pyroxylin, as the base. This is not a single chemical substance but a series of nitrocelluloses containing 11 to 12.5 per cent nitrogen and often some oxycellulose or hydrocellulose and their nitrates. Therefore, the basic substance employed in nail lacquers is variable in composition. This is of significance because slight alterations in chemical structure may produce a variation in eczematizing property. Solvents must be used in which to dissolve or suspend the pyroxylin and other ingredients. No single solvent is satisfactory. Mixtures of solvents with high and with low boiling points are generally employed. If a lacquer dries too rapidly, the resulting drop in temperature causes moisture from the atmosphere to condense on the film. There are at least fifteen different solvents in various combinations employed for this purpose. Plasticizers are added to promote flexibility. There are at least twenty-five combinations of these in use. These substances prevent cracking and chipping. The addition of gums and resins increases the adhesive quality and adds to the luster. Color is produced by the addition of sudan pigment and zapon-proof coloring substances. To mask the odors of these mixtures, perfumes

6. Ellis, F. A., and Kirby-Smith, H.: Contact Dermatitis Due to Nail Polish, J. A. M. A. **116**:45 (Jan. 4) 1941.

7. Greenbaum, S. S.: Leukoplakia of Unusual Origin, Arch. Dermat. & Syph. **33**:538 (March) 1936.

8. Van Ostrom, W., and Anderson, R. J.: Nail Polish, Drug & Cosmet. Industry **39**:52, 1936.

9. Kolish, J.: Tested Formulas for Manicure Products, Drug & Cosmet. Industry **41**:492, 1937. Harry, R. S.: Compounders Corner, ibid. **45**:229 and 613, 1939.

are frequently added. Table 1 lists some of the more common ingredients in the various classifications. It must be apparent that nail lacquers are highly complex mixtures containing a large number of potential eczematizing substances. The formulas are constantly changing as improvements are introduced.

The identical cellulose nitrates used in nail lacquers are also widely used—usually in combination with solvents, plasticizers, gums, varnishes, resins and pigment—in industry, for instance, in the manufacture

TABLE 1.—*Substances Which May Be Present in Nail Lacquer*

Cellulose Nitrates	Solvents	Plasticizers, Gums and Resins	Pigments	Perfumes
(Pyroxylin)	Methyl, ethyl, butyl and isopropyl alcohols	Butyl carbitol	Sudan	Many
		Buty carbitol acetate	Zapon-proof (resistant to cellulose nitrates)	
Blends of various viscosities	Methyl, ethyl, butyl, amyl, isopropyl, propyl, cyclohexyl and ethylglycol acetates	Dibutyl phthalate	Titanium white	
		Dibutyl tartrate	Zinc oxide	
		Butyl stearate	Ultramarine	
		Amyl stearate	Ochre earths	
		Triamyl citrate	Rouge	
		Diamyl phthalate	Vermillion	
		Carbitol acetate	Cadmium yellow	
	Glycol monoacetate	Resorcinol diacetate		
	Carbitol	Triphenyl phosphate		
	Tolnol	Tricresyl phosphate		
	Acetone	Dimethoxytetra glycol		
	Butanol	Dipropylene glycol		
		Phenylcellosolve		
		Benzylcellosolve		
		Triacetin		
		Castor oil, camphor		
		Copal, colophony		
		Shellac, benzine resins		
		Chlorocompounds		
		Ester gum, gum mastic		
		Gum sandarac		
		Dammar gum		
		Benzoin		

of automobiles, airplanes, steel and wood products.[10] The following common objects are coated with these substances:

Imitation leather (including patent leather): handbags, purses, belts, jackets, etc.

Glass: beads, mirrors, chandeliers, etc.

Metal: jewelry, cigaret cases, vanity cases, bronze figures, furniture, silverware, lighting fixtures, hairpins, etc.

Wood: jewelry, brush handles, broom handles, umbrellas, walking sticks, pencils, pens, furniture, floors, woodwork, cigaret boxes, etc.

Miscellaneous: porcelain, celluloid playing cards, drawings, pictures, toys, buttons, straw hats, cigar tips, collar buttons, buckles, leather objects, water-proof fabrics, etc.

In this paper we wish to present an analysis of our first 100 cases of dermatitis due to nail lacquer.

10. Wilson, S. P.: Pyroxylin Enamels and Lacquers, New York, D. Van Nostrand Company, Inc., 1927.

The youngest patient was 19 and the oldest 77 when the dermatitis first appeared. The vast majority of patients were in the 20 to 40 age group, as would be expected. There was only 1 man in the entire group. He had received weekly applications of colorless nail polish.

The distribution of the eruption is of great interest, and localization occurs in the areas of most frequent contact with the finger nail.

TABLE 2.—*Involvement of the Eyelids in One Hundred Cases of Dermatitis Due to Nail Lacquer*

Involvement of the Eyelids		Number of Cases
Total		78
With involvement of other parts	40	
Without involvement of other parts	38	
Eyelids involved		
Both upper		40
Right upper alone		9
Left upper alone		4
Both upper and lower		25

TABLE 3.—*Distribution of Eruption Other Than on the Eyelids in One Hundred Cases of Dermatitis Due to Nail Lacquer*

Eruption Elsewhere Than on the Eyelids		Number of Cases
Total		62
With involvement of eyelids	40	
Without involvement of eyelids	22	
Distribution of lesions		
Neck		30
Cheeks and nose		17
Shoulders and chest		14
Pinna		12
Lips and angles of mouth		7
Chin		7
External auditory canal		5
Trunk and thighs		5
Arms and forearms		5
Forehead		4
Anogenital areas		3
Fingers and dorsa of hands		2
Axillas		2
Legs		1
Nostrils		1

Although the habits of women vary greatly, there are some entirely conscious and other unconscious finger nail contacts which every woman makes more or less frequently with her skin. The eyelids, especially the upper lids, are rubbed frequently, and a careful scrutiny of this action shows that a portion of the nail slides back and forth across the thin skin of the upper eyelids. In 78 of the 100 cases reported here, the eyelids were involved (table 2). Both upper lids were involved in 40 cases, the right upper lid alone in 9 and the left upper lid alone in 4. Both upper and lower eyelids were involved in 25 cases. In only 22 cases were the eyelids uninvolved. Table 3 summarizes the

distribution of the dermatitis on parts other than the eyelids. Forty, or approximately two thirds, of these patients also showed involvement of the eyelids. The one third, or 22, that did not show involvement of the eyelids we believe to be of great importance. It is easy enough to suspect nail lacquer as the cause of the dermatitis on the eyelids when it is realized that in well over 90 per cent of our cases the condition was due to nail lacquer. However, when the dermatitis is distributed on the other areas, as summarized in the table, including such unusual locations as the chest, trunk, thighs, arms, anogenital areas, axillas and hands, it behooves the dermatologist to include nail lacquer in any list of possible causes.

The common habit of resting the face and neck on the back of the flexed fingers undoubtedly accounts for the frequency of distribution on these parts. Arranging the collar or the neck of a dress accounts for the distribution on the neck and extending down over the clavicular surfaces. Arranging or fussing with the hair, an extremely common and usually unconscious habit with women, brings the thumb nail in direct contact with the nuchal area. Wire hairpins coated with lacquer frequently account for a dermatitis extending up over the occiput. Removing wax, scales and crusts from the external ear and external auditory canal by the use of a finger or a wire hairpin explains many cases of dermatitis of these areas. A patch of dermatitis in front of one or both ears occasionally appears in women who wear glasses, the bows of which must be adjusted over the ears. In addition to the areas listed in table 3, we have had some cases of extensive confluent dermatitis, others of generalized itching and others in which patches were scattered indiscriminately over the body.

The subject of dermatitis of the eyelids deserves special consideration. In our experience it is rare in men and common in women. In our opinion a patch of dermatitis on one or on both upper lids is in more than 90 per cent of cases due to nail lacquer. When both upper and lower lids are involved, there is more chance that the cause is something other than nail lacquer, such as medications used about the eye and in the conjunctival sac and also medications applied elsewhere on the body and transferred to the eyelids by the fingers. Dermatitis of the eyelids due to contact with metal eyelash curlers and cosmetic preparations develops at the exact point of contact with these substances. We have had a number of cases of dermatitis of the eyelids due to phosphorus sesquisulfide transferred to the lids by the fingers after contacting the heads of matches. With the popularity of cigaret lighters, this condition has not been seen so frequently in the last few years.

Clinical observation has convinced us that the distribution of the eruption in a case of dermatitis of the eyelids due to nail lacquer from its onset through to its full development is somewhat different from

that in a case of dermatitis of the lids due to other causes. In the former case, the patch on the eyelids almost always begins as a small dry erythematosquamous area, the size of a pea, about ½ inch (1.3 cm.) from the inner canthus of the eye and midway between the eyebrow and eyelashes and gradually extends laterally, usually for not more than ¾ inch (2 cm.). Periodicity is also of importance, but too much attention should not be given to this factor. Often the patient will give no history of complete involution or exacerbation.

In most cases the dermatitis was of a low grade erythematosquamous variety. In 85 of the cases no macroscopic vesiculation was noted. In some there was considerable edema, with dermatitis about both eyelids. The dermatitis usually occurred in small areas or patches. In only 3 or 4 instances was there a widespread, confluent dermatitis on the face, neck and shoulders.

The average duration of the dermatitis at the time of examination was twelve and eight-tenths months; the shortest duration was one day and the longest eight years. In a case of a long-standing condition a history of repeated attacks was the rule.

In view of the fact that the use of colorless nail lacquer has been widely advertised in recent months, we predict an increase in the number of male patients with this condition.

When the use of nail polish was abandoned the dermatitis disappeared in an average time of three and one-half weeks, the shortest period being one week and the longest eight weeks. In many cases, either owing to skepticism on the part of the patient or at our advice, the nail polish was again tried, with a recurrence of the dermatitis. When recurrences took place in the absence of nail polish, some other cause was suspected, searched for and eliminated when possible. In a number of puzzling cases, nail polish was only one of the allergens found to be the cause of the dermatitis. One case of this kind was that of a woman with a recurring dermatitis of the cheeks, neck, shoulders, eyelids, ears, upper part of the trunk and arms. She had been hospitalized for several weeks, during which time she had had several exacerbations. The dermatitis improved greatly when she went away from home for a period of ten days, and there was a sudden recurrence on the day she returned. Finally, discontinuance of the use of cosmetics on the part of her three devoted daughters caused the dermatitis to subside, but it was not until a patch of dermatitis appeared on her leg after she had applied nail polish over the area to stop a run in her stocking that the final and apparently most important allergen was discovered. It is interesting to note that previously she had given a negative reaction to a patch test with this substance on her back.

When the dermatitis is localized to one or two or a few small areas about the eyelids, we believe that patch tests are of doubtful value.

When the dermatitis is more extensive with a more generalized distribution of epidermal hypersensitivity, patch tests may be of great value. In a number of cases of dermatitis of one or of both eyelids in which the condition was proved later to be due to nail lacquer, we painted a small amount of the substance adjacent to the eyelid, with negative results. Repeatedly, in proved cases we have observed negative results of patch tests on the back or arms. However, in a recent series of 16 cases of nail lacquer dermatitis, 15 patients gave positive reactions to patch tests with their own nail lacquer. In only 1 was the dermatitis confined to the eyelids. In our opinion there is no substitute for careful clinical observation following the withdrawal of the offending allergen. Another point of possible importance is the observation that the reaction to a patch test is more apt to be positive if the lacquer is applied to a piece of gauze or linen, in the usual manner of patch tests, and not painted directly on the skin. The dried lacquer on the gauze or linen causes some rubbing and scratching of the surface of the skin. The skin is protected by a layer of sebaceous material and sweat which prevents close contact of the lacquer with the epidermis if the lacquer is painted on the skin. Whether a dermatitis is due to the pure cellulose nitrate, the solvent, the pigment, the plasticizer or the perfume we believe to be of little importance in the individual case. It is obviously impossible to test a patient with all of the substances which may be present in a given sample of nail lacquer. From a clinical standpoint, testing the patient with the actual nail lacquer used and also with colorless lacquer gives all of the information necessary. Originally we felt that there would be many patients who would react to both lipstick and nail lacquer. However, in the entire series there was only 1 patient who gave positive reactions to tests with both substances. She had a dermatitis of the lips due to lipstick and a dermatitis of the eyelids due to nail lacquer. Our experience indicates that the pigment is seldom the cause of the dermatitis.

One of the most important aspects of this study was the implication which it had in regard to many other cases of dermatitis of obscure causation in babies, children and adults. Many of the objects listed as common sources of contact with cellulose nitrate lacquer are objects of everyday contact. We refer especially to toys and playthings handled by babies and children as a potential cause of dermatitis of the lips, cheeks and surrounding areas. Pencils, pens and other objects commonly inserted in the mouth by children and adults must also be considered. The arm of a lacquered chair or the top of a desk may explain many cases of chronic eczema of the contact area on the forearm. With the rapidly expanding use of cellulose nitrate lacquers, the importance of investigation along this line is obvious.

SUMMARY AND CONCLUSIONS

1. Nail lacquers are highly complex mixtures containing many ingredients which are potentially eczematizing.

2. Similar lacquers are widely used in industry and are applied to the surface of many objects in common usage. Their importance as possible eczematizing agents should not be overlooked.

3. Dermatitis due to nail lacquer is common and will probably become more so, especially in men.

4. Nail lacquers are the most frequent cause of dermatitis about the eyelids in women and should be considered as possible causes of dermatitis of the face, neck, cheeks, ears, ear canals, shoulders, chest and lips.

5. Less common sites of dermatitis due to nail lacquer are the thighs, arms (particularly the cubital areas), axillas, anogenital area and legs and the general body surface.

6. In all cases of dermatitis of obscure causation nail lacquer should be suspected and eliminated.

7. Dermatitis from nail lacquer is usually of a patchy erythemato-squamous variety. Macroscopic vesiculation is the exception rather than the rule.

8. Patch tests in cases of dermatitis due to nail lacquer are of doubtful value. They should not supplant careful clinical observation.

ABSTRACT OF DISCUSSION

DR. JAMES HERBERT MITCHELL, Chicago: There are one or two points I should like to bring out from my own experience. In the matter of the negative reaction to a patch test, I had 2 patients recently, from out of town, who gave positive reaction to patch tests with three different preparations and with the colorless lacquer.

On another patient, who lived in the city, I made patch tests with five different preparations, to all of which the reactions were negative. Then I made patch tests with about fifteen different cosmetics and five different soaps. The reactions were negative to all. I was at my wit's end and unable to account for the patient's dermatitis. She was getting impatient. I finally said to her, "Now, you are doing something I don't know about, and I should like to have you cogitate and ransack the bathroom." She went home, called up and said that she had forgotten to tell me that she was using a hand cream, but that she never put it on her face. It was found that the purchase of the cream coincided with the appearance of the dermatitis on the lids. Patch tests with that hand cream gave me the solution to the problem.

During the first year of the appearance of paper cleansing tissues I had a patient with dermatitis of the lids. She was a very intelligent person and had cooperated in every way. Again I said to her, finally, in despair, "You are doing something I don't know about." Then she told me that she had not thought to say that she used green cleansing tissue. That was the cause of her dermatitis. Cleansing tissue has proved to be the cause of dermatitis in a number of other cases of dermatitis of the lids.

In some instances of dermatitis of the eyelids I think perhaps it might be well to apply nail lacquer directly to the upper fold of the lid, after the dermatitis has subsided. In some cases a positive reaction is obtained only in that way.

In regard to the commonly observed patch of lichen simplex chronicus in the occipital region, it was a surprise to me to be able to prove recently that such an area which had been treated by the referring physician with roentgen rays to the point of probable permanent alopecia was a fixed eruption due to phenolphthalein.

DR. H. J. PARKHURST, Toledo, Ohio: This condition was first brought to my attention by Dr. Sulzberger in his lecture on dermatitis venenata at the Philadelphia meeting of the American Academy of Dermatology and Syphilology. Since that time I have observed 3 cases in my practice in which the eyelids and the front of the neck were involved. I might say that in 2 of these cases there was a striking resemblance to a fixed eruption due to phenolphthalein.

DR. J. F. BURGESS, Montreal, Canada: I confess that I recognized my first case of this condition a little over a year ago. Since that time I have encountered 35 cases, most of them within the last few months. The clinical picture has been well described, and it certainly fits in with my findings. I found, for instance, that patients who are sensitive to one brand of nail polish can seldom use another brand without getting severe exacerbations. I had one patient who felt she was "naked" unless she used nail polish, and she proceeded to try in turn all the nail polishes she could, with disastrous results as far as her skin was concerned.

Recently I have been interested in trying to find out the ingredient which possibly might be the important factor. I realize from Dr. Osborne's listing of the many substances in nail polish how difficult that is. However, I picked out one particular brand of nail polish and gave a series of 22 patients patch tests with about eight different ingredients, and some of these substances contained a number of allied products, such as dyes. My findings, briefly, are as follows: 1. The solvents play no part in the causation of the eruption, patch tests with them eliciting negative reactions. 2. The dyes elicited mild reactions only, such as erythematous or erythematoedematous reactions, and these occurred in only about 45 per cent of the cases. I am inclined to discount the importance of the dyes. 3. The resinous substances elicited strong reactions, which were vesicular or sometimes exudative, in about 60 per cent of the cases, but in 40 per cent of the cases there were negative reactions. Nitrocellulose in solution caused strong reactions, vesicular or sometimes exudative, in 100 per cent of the cases.

One would feel that one was dealing with a primary sensitization due either to nitrocellulose solution or to resinous substances, or to the combined action of these products. It is difficult to see why nitrocellulose should give such uniformly positive results. Recently I had occasion to find out something which I did not know, and that is that in this nitrocellulose solution benzene is added. I tested a series of normal persons in the clinic and found that about 65 per cent gave minimal reactions to benzene, which compares well with the number of reactions to nitrocellulose solution in a similar series of normal persons. In a few persons with nail polish dermatitis vesicular and exudative reactions occurred from the benzene; so there is a possibility that benzene in nitrocellulose solution may also be a factor of some importance.

Therefore, I rather feel that possibly two factors are the more important in this sensitization, namely, the resinous substances and the nitrocellulose lacquer, which also may contain benzene as one of its ingredients.

DR. GEORGE M. MACKEE, New York: The author called attention to the fact that, among many other things, lacquer dermatitis of the eyelids and other locations may consist of a continuous dermatitis or there may be exacerbations. I have had a few patients who have permitted the application of a small patch test on the eyelid after the eruption has subsided. In some instances the reaction has been positive and in some instances negative during the period of remission. I was wondering whether that difference might be due, perhaps, to a faulty method of applying the patch or whether there is such a thing, in Dr. Osborne's opinion, as fluctuating allergy.

Does Dr. Osborne believe that nail polish can produce pruritus without dermatitis?

DR. JOHN G. DOWNING, Boston: I think this paper brings out an interesting factor, and that is as to the use of the patch test. Every week I change my ideas about patch tests. I have learned that many things are not sensitizers but primary irritants when enclosed.

For instance, when one encloses lacquers, rubber cements and the group of substances containing volatile solvents they cause a primary irritating action. They should not be enclosed but should be merely dropped on the skin. If a patient is sensitized to rubber cement, all one has to do is to apply it and leave it on overnight, simulating the exposure all day in handling rubber cement. The same holds true for lacquers.

A nurse on surgical duty, who wore a mask over her lips most of the day, had a persistent dermatitis of the eyelids. She became sick with tonsillitis, and her dermatitis cleared up during her stay in bed. When she returned to the operating room, the dermatitis of the eyelids recurred, and her lips also became involved. A patch test with her lipstick elicited a positive reaction. Merely touching it to her skin without an occlusive dressing gave a similar reaction. The girl was getting her dermatitis of the lids from breathing up into the mask, blowing the volatile solvent in the lipstick onto her lids. Later when she became more sensitized, subsequent reexposure produced the cheilitis.

DR. RALPH HOPKINS, New Orleans: I thought it rather unusual that lacquer should produce a dermatitis of the external surface of the ear lobe and that the way it occurred was worth mentioning. I had been treating a young woman with an apparent contact dermatitis on one cheek for some time with indifferent success. One day she had on the lobe of each ear a circular patch, sharply defined, in the exact area which her earrings touched. She had been wearing these earrings for four or five years; they had become rusty, and to "revive" them she painted them with the lacquer which she used on her finger nails. While she was sitting in the office she put her hands to her face (resting chin in hand with her flexed fingers touching her cheek), and the dermatitis on the face corresponded exactly with the part of the cheek with which her finger nails were in contact.

DR. RICHARD L. SUTTON JR., Kansas City, Mo.: A curious feature of nail lacquer dermatitis is its sharp demarcation and discrete character. One would expect a dermatitis provoked by something that is more or less smeared over the skin to be more widespread and less discrete than it is. That, to my notion, is one of the best diagnostic features of it. I wonder if Dr. Osborne might explain this. In the first case I encountered the condition was discrete and consisted of four separate patches of contact dermatitis on each elbow. The patient, a school teacher, was accustomed to standing with her arms folded.

I have been led to believe that the chemical used for removing the lacquer is also sometimes important. The dermatitis will flare at the time the lacquer

is removed. It may be, of course, that it is simply liquefied and made available for deleterious effect at the time of removal, but I have suspected the remover of being a cause in itself.

I believe with Dr. Downing that the noxa is sometimes air borne. I saw a girl in a boarding school whose condition improved temporarily when she removed her nail polish at my request, but later she had violent exacerbations, which were attributable to her roommate's enthusiastic interest in various lacquers.

Nail lacquer will cause disease in surprising locations, as exemplified by one unmarried woman I saw who had pruritus vulvae caused by it.

It will sometimes provide a complication of other diseases. A girl of 10 years and her mother came to me with scabies. Routine sulfur treatment cured the mother, but the child's condition did not improve. She continued to have the pruritus and eruption, but the eruption seemed on close examination to have changed character and now simulated that of poison ivy. Where she scratched the scabies, nail lacquer dermatitis developed. After removal of the polish her "scabies" disappeared. She had used nail lacquer as a toy, as a child would, for a long time before she had scabies, but it was as a complication of the scabies that the lacquer dermatitis developed.

Dr. Henry D. Niles, New York: I should like to discuss two or three clinical features which have not as yet been mentioned. I was about to comment, as Dr. Sutton did, that the patches usually are rather sharply circumscribed. I think that is the reason why, as some of the speakers mentioned, they are mistaken at times for a phenolphthalein eruption. They are often the shape of the finger nails themselves, which I think is characteristic.

Another clinical feature I have noticed is that in many of the patients the lesions are more on one side of the neck than they are on the other. If the patient lies with her hand under her head at night and she sleeps on her right side, there are more lesions on the right side; if she lies on her left side, there are more patches on the left side of the neck.

Another feature of this eruption is its periodicity. There are many older women who use nail polish only on special occasions. For this reason, their eruption will come and go. This makes it difficult to find the cause, as on such occasions they have candy, cake and sometimes cocktails, which they do not have ordinarily, and they are prone to attribute their eruption to some dietary change rather than to the nail polish.

Dr. Earl D. Osborne, Buffalo: I feel, as Dr. Downing does, that the interpretation of the patch test is a job for an expert and not for an ordinary physician or for any tyro. Many results are difficult of interpretation, depending on the method of performing the test, and the location on which the patches are applied.

I have no explanation for the variation in reaction to patch tests on different areas except that common experience shows that the length of time of application, the friction produced by it, the thinness of the horny layer and the amount of sweat in a given area at the time of application are important. The dermatitis occurs on the eyelids because, among other factors, the horny layer is extremely thin, there is usually quite a bit of moisture present and friction is caused by the nail.

In reply to Dr. MacKee's question regarding pruritus without dermatitis, I have not seen any patient with generalized pruritus or localized pruritus that I could attribute as due to nail lacquer or any other lacquer. I have been looking for that, especially from inhalation, in persons employed in the paint and lacquer industry.

The discreteness of the eruption, I think, is fully accounted for by the fact that the eruption must be due to the actual contact with the nail.

By analyzing the habits of women, one can explain all these different locations. Pruritus vulvae and pruritus ani, with usually a low grade dermatitis, due to nail lacquer, I believe, should be looked for more frequently. We, too, have had some cases of dermatitis on the elbows due to crossing the arms.

Regarding the substance in nail lacquer that produces the sensitization, we have gone through a long series of patch tests in these cases, and we have come to the conclusion that it is almost hopeless in the individual case to find the exact substance unless it is readily apparent that the condition is due to the pigment itself. From our experience, we believe that the sensitizing agent is usually a resin or plasticizer, less frequently the cellulose nitrate itself and seldom the pigment.

ERYTHEMA PALMARE AND NAEVUS-ARANEUS-LIKE TELANGIECTASES

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Erythema palmare hereditarium is the name that was given by Lane [1] in 1929 to a condition he observed in 2 men. Both had had red palms as long as they could remember, and other members of their families presented similar changes. The condition was characterized by bright erythema of the palms which was sharply limited at the wrist line and along the sides of the hands. In one of the patients the redness extended onto the dorsa of the terminal phalanges. There were no other changes in the skin and no subjective symptoms.

Since this first description only 9 other cases have been reported, although the condition is probably not rare, as was brought out in the discussion of Lane's paper. During the past two years we have seen 9 patients with palmar erythema, all of whom were women. In 4 the condition occurred during pregnancy and was associated with the appearance of telangiectases of the nevus araneous type on the arms, neck and face. We have not been able to find this association of palmar and in some cases plantar erythema, naevus-araneus-like lesions and pregnancy described in the literature; hence we feel that a report is justified.

REPORT OF CASES

ERYTHEMA PALMARE AND NAEVUS-ARANEUS-LIKE TELANGIECTASES

CASE 1.—Mrs. N. S., aged 26, was referred to the dermatologic clinic in the ninth month of her fourth pregnancy because of redness of her palms (fig. 1) and soles and small erythematous telangiectatic lesions on the arms, face and neck. The red palms had appeared in the fifth month of the pregnancy, and the telangiectases began to appear about one month later. The soles were involved to a lesser degree. There were no other observable changes in the skin and no subjective symptoms. The patient stated that during her second pregnancy the palms had also become red at about the same time but that no red spots were noticed on other parts of the body. The hands returned to normal after delivery. All her pregnancies were otherwise normal.

From the Section of Dermatology of the University of Chicago, The School of Medicine.

1. Lane, J. E.: Erythema Palmare Hereditarium, Arch. Dermat. & Syph. **20**: 445 (Oct.) 1929.

The patient had had the usual childhood diseases and had had pneumonia at 15 years of age. When 24 years of age she was examined because of a sudden loss of weight, the cause of which was not discovered. There was no history of familial disease; no other members of the family were known to have had a similar condition. One sister took thyroid substance because of obesity. The Kolmer and Kahn reactions of the patient's blood serum were negative.

The patient was observed for eight months after delivery. One week after delivery the erythematous palms were definitely paler, and many of the individual lesions present elsewhere had disappeared. The color gradually faded during about four weeks and then remained stationary. When she was last seen there was only

Fig. 1 (case 1).—Erythema palmare.

one rather large naevus-araneus-like lesion in the right clavicular region. This had an elevated central punctum which showed arterial pulsation on glass pressure.

Case 2.—Mrs. G., aged 23, a housewife, was first seen by us while she was in the Chicago Lying-in Hospital of the University of Chicago for her second delivery. During the second month of her pregnancy she had noticed redness developing on the ulnar side of both palms and gradually spreading over the entire palms. The discoloration was blotchy and varied somewhat from time to time. There were no subjective symptoms, and the soles were normal. The patient had a naevus-araneus-like lesion on each forearm and a few small dilated vessels on the neck. She did not know whether these had been present before she had become pregnant. She was sure, however, that she had had no similar changes during her first pregnancy.

There was no history of any serious illness. No member of the family had a similar condition. Two sisters had had children without having red palms. The Kolmer and Kahn reactions of the blood serum were negative; the urine was normal on examination, and the blood count was normal.

Nine days after a normal delivery the palms had faded somewhat. The patient was not seen again.

CASE 3.—Mrs. F., aged 29, was seen while hospitalized for her first delivery. Her husband had first called her attention to her red palms during the fourth month of pregnancy. She also noticed the appearance of several red spots on her arms, but some of these had been present before she became pregnant. Her hands were slightly swollen for some time before term; but there were no subjective sensations, and the soles were not involved.

The patient had had diphtheria at the age of 6 years and had had chorea at the age of 11 years, which was followed by the development of a heart murmur. She had had urticaria several times. There was no history of familial disease, and no one else in the family had a similar condition.

The Kolmer and Kahn reactions of the blood serum were negative; the urine showed slight reaction for albumin, and the blood count was normal.

On the day following delivery the hands were definitely paler, and when she was seen for the last time six weeks later the palms were only slightly erythematous.

CASE 4.—Mrs. E. M., aged 31, was first seen three days after the birth of her second child. She had first noticed red palms a few weeks after the birth of her first child two years previously. The redness had faded somewhat and then had become more intense during her second pregnancy. Red spots had developed on her arms, face and neck during the latter part of pregnancy.

The patient had had no serious illness but was taking thyroid for treatment of obesity.

The patient's mother was one of nine children, six of whom had red palms. One of the patient's three brothers has the same condition.

While the patient was in the hospital after the delivery the color of the palms and the naevus-araneus-like lesions faded slightly. The patient reported after two years that the palms were still definitely redder than normal. She noticed that the red spots on her arms, face and neck appeared during the summer when she became sunburned and tended to disappear in the winter.

ERYTHEMA PALMARE

CASE 5.—Mrs. W., aged 37, a Jewish housewife, was first seen while she was in the hospital during her third pregnancy. The patient had been a beautician and had noticed for ten or twelve years that her palms became red when placed in hot or cold water. Recently this change was associated with a mild burning and slight swelling of the hands. In 1932 she had had two miscarriages, at two and at three months, but had noticed no change in the palms. During the next five years the erythema had become more constant, but there had been no particular change during the current pregnancy. There had been no other changes in the skin of the palms, and there were no lesions elsewhere. The soles were not affected. She had had a renal stone removed in 1933. She had one brother who also had red palms.

The Kolmer and Kahn reactions of the blood serum were negative. The urine showed traces of albumin, red blood cells and hyaline and granular casts.

Her third pregnancy was terminated by cesarean section. Seven weeks after delivery there was no significant change in the appearance of her hands.

CASE 6.—Mrs. L., aged 36, a housewife of German extraction, first noted redness of her palms five or six years before she was first seen. She had had two pregnancies, in 1927 and in 1929, but stated the belief that the palms had not been red at either time. The condition caused no symptoms, and she had noticed no other red spots on the body. The soles were not involved. The color was brighter during warm weather. She had had a pelvic operation in 1930, and subtotal hysterectomy had been performed in 1938.

The patient's mother had the same condition of the palms, which the patient thought had been present for only a few years. No other person in the family was known to have it. The mother also had noticed occasional blanching of one or more fingers, not necessarily related to exposure to cold.

The Kolmer and Kahn reactions of the blood serum were negative; the urine was normal on examination, and the blood count was normal.

CASE 7.—Mrs. B., aged 35, a housewife, came to the dermatologic clinic because of leukoplakia buccalis. Erythematous palms, which had been present as long as she could remember, were noticed during routine examination. The color varied somewhat from day to day and was more intense in warm weather. She had had one induced abortion at one month and had noticed no change in the palms at that time. She had noticed no red spots on the rest of the body, and the soles had not been involved.

She had had influenza, in 1928, but no other illness. One younger sister had a similar cutaneous disease; three other sisters and one brother did not. Two of the sisters had children but had noted no changes in the palms during pregnancy.

The Kolmer and Kahn reactions of the blood serum were negative, and the urine was normal on examination.

CASE 8.—Mrs. L., a widow aged 59, came to the clinics because of typical symptoms of hyperthyroidism. She had first noticed red palms five or six years previously. There were no subjective symptoms; the soles were normal, and no naevus-araneus-like lesions were found.

The patient had had rheumatic fever at the age of 19, and arthritis had developed at the age of 35. She had had no other illness until the present condition began two years before attending the clinics, and she had never been pregnant. There was no history of familial disease.

The Kolmer and Kahn reactions of the blood serum were negative; the urine was normal on examination, and the blood count was normal. The basal metabolic rate was between + 30 and + 40 per cent on several occasions. A diagnosis of hyperthyroidism was made.

CASE 9.—Mrs. E. B., aged 50, a switchboard operator, first noted that her palms had become unusually red about one year before admission. The degree of erythema had varied from time to time. She had experienced no subjective symptoms. She had lost 62 pounds (28 Kg.) in three years and had had polydypsia for one and one-half years. She had always been unusually nervous and had perspired a great deal. She had noted severe palpitation and intolerance to heat, associated with a choking sensation, for one year.

She was first seen in the surgical clinic on Sept. 11, 1940, complaining of pain in the lower part of the abdomen of six weeks' duration and of a mass bulging from the vagina. Gynecologic examination revealed cystocele, rectocele and bilateral adnexal masses. Dermatologic examination revealed erythema of the borders and over the thenar and hypothenar eminences of the palms, with a pale triangle in the center.

Urinalysis revealed 4 plus reduction. The blood sugar (fasting) amounted to 165 mg. per hundred cubic centimeters. Two examinations for blood cholesterol revealed 115 and 128 mg. per hundred cubic centimeters. The value for blood urea nitrogen and the urea clearance were normal. The basal metabolic rate varied from + 42 to + 29 per cent.

Diagnoses were made of diabetes mellitus and hyperthyroidism. The diabetes was controlled, and thyroidectomy was performed. The patient stated the belief that the palms have become less erythematous since she has been hospitalized.

NAEVUS-ARANEUS-LIKE TELANGIECTASES

Case 10.—Mrs. S., aged 28, a housewife, was first seen in the ninth month of her second pregnancy. She stated that during the third month she had noticed red spots appearing on the upper part of the right arm. They consisted of groups of small dilated blood vessels some of which had a small central red dot. These spots gradually increased in number and spread down the arm. A few appeared on the left arm and on the neck. Except for some swelling of her hands and feet during the final months, her pregnancy was normal. The palms showed no abnormality.

The patient had had no serious illness. For five years she had taken thyroid because of rapid gain in weight and a basal metabolic rate of — 37 per cent. Her first pregnancy, during which she had noticed no cutaneous changes, had been terminated at three months. There was no history of similar cutaneous disease in the family. The results of physical examination were essentially negative. The Kolmer and Kahn reactions of the blood serum were negative.

Six months after delivery the lesions were still visible, but the color had faded considerably.

Case 11.—Mrs. I. O., a 27 year old Jewish housewife, was observed in the dermatologic clinic during her first pregnacy because of rosacea-like tuberculid, for which she had been receiving treatment. She had had several small red spots on her hands and arms for years, but at about the fourth or fifth month of her pregnancy these had increased greatly in number and become much more prominent. She felt well during the pregnancy. The palms were never red. There was no family history of the condition.

After the patient was delivered of a stillborn child, the lesions gradually faded, some disappearing completely. The rosacea-like tuberculid also improved after delivery. Biopsy of one of the lesions on the left arm was made about one month before term. The section is described in another part of the paper.

DESCRIPTION AND COURSE OF THE DISEASE

The symmetric erythema of the palms had an almost identical distribution in all 9 cases and was similar to that in the cases previously reported. It was most pronounced on the thenar and hypothenar eminences, along the bases of the fingers and on the tips of the terminal phalanges. A central triangular area with its apex toward the wrist was usually spared or was definitely lighter in color than the rest of the palm. The margin of the erythematous zone was sharp at the ulnar side of the wrist line and along the sides of the hand at the point of transition from the palmar skin to the skin on the dorsum of the hand. The redness extended onto the dorsum of the terminal phalanges in some of the

patients. In 1 instance the soles were involved over analogous areas, but they were not nearly as red as the palms.

The color was bright red, simulating at first glance the brilliant erythema of an acute inflammatory process. It would vary in intensity from patient to patient and at different times in the same patient. It disappeared completely on glass pressure. There was a coarse mottling of the erythema suggesting an exaggeration of the normal mottling of the palm. There was no hyperhidrosis, and only 1 patient (case 5) had any subjective symptoms.

The telangiectases noted in the women in whom the palmar erythema was associated with pregnancy were chiefly of the naevus araneus type. However, some were only small macular telangiectases without a definite central punctum. They varied in number from three or four to thirty or more, were distributed over the hands, arms, neck, face and upper part of the chest and varied in size from 2 to 10 mm. in diameter. In the larger ones the central punctum was elevated and showed arterial pulsation on glass pressure. Many of the lesions showed an anemic halo 3 to 4 mm. wide. This became more noticeable when the patient was flushed. Two patients are described (cases 10 and 11) in whom only telangiectases on the arms, chest, neck and face were evident.

Only 1 patient could describe the development of the erythema (case 3). She first noticed it on the proximal portion of the hypothenar eminence. From there it spread distally and to the thenar eminence, finally assuming the distribution described. One other patient, not included in the series, who was seen only once in about the fourth month of pregnancy, had symmetric involvement of only the hypothenar eminences.

In patients whose condition was of long duration and unrelated to pregnancy, there was no change during the period of observation. Exposure to heat accentuated the color, and some patients had noticed that the palms became more erythematous in the evening. In those whose condition began during pregnancy, the hands became paler at a time varying from a few hours to seven days after delivery, but in none of them did the color fade entirely during the period of observation, which varied from ten days to two years.

The naevus-araneus-like lesions usually were noticed between the second and fourth month of pregnancy and, like the palms, they faded after delivery, some disappearing completely.

CAPILLARY STUDIES AND BIOPSY

Four patients (cases 1, 6, 7 and 8) were studied by the capillary microscope. Both the nail fold and the palm were examined.

In the nail fold the findings varied considerably. In case 1 there were some increased tortuosity of the vessels and slight dilatation, espe-

cially of the venous side (fig. 2). According to Baer and Reis,[2] this condition may be seen in normal pregnant women, but it is more common in patients with toxemia of pregnancy.

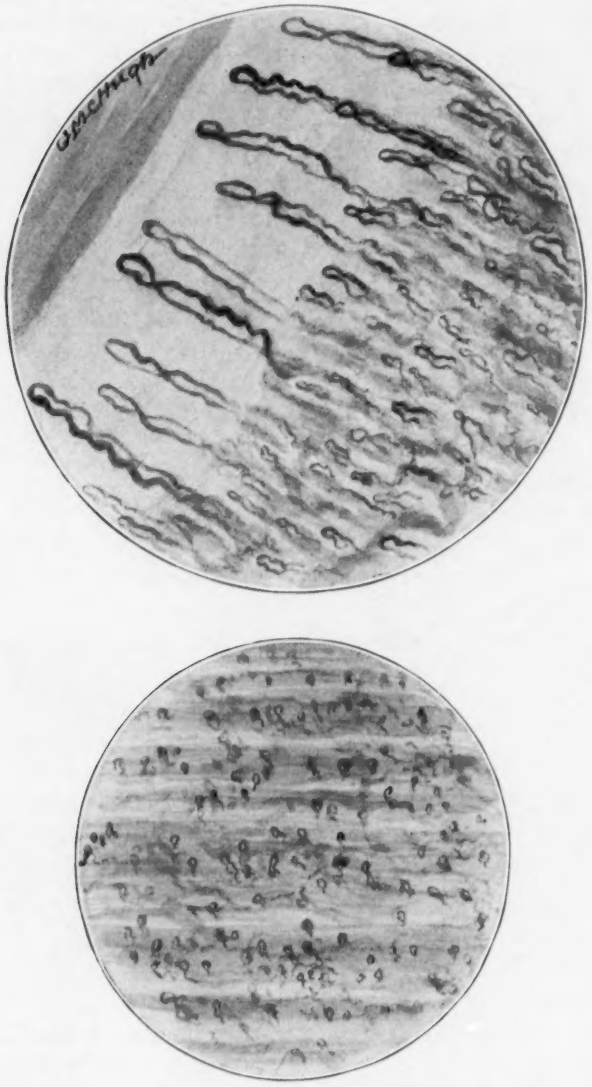

Fig. 2 (case 1).—Capillary microscopic picture of nail fold and palm.

A definite abnormality was seen in case 6. There were an increase in the tortuosity of the capillaries and also decided dilatation of the

2. Baer, J. L., and Reis, R. A.: Capillaries in Pregnancy, J. A. M. A. **82:** 526 (Feb. 16) 1924.

venous side in many of the loops, extending as far centrally as the vessels could be seen and over the arch to the arterial side.

In case 7 the nail fold was difficult to examine because it was separated from the nail. However, the capillaries seemed to be more tortuous than normal, and many showed dilatation of the arch.

In case 8 capillary loops in the nail fold were long and narrow, with no tortuosities. There was little variation between the venous and the arterial side of the loop. This patient had limited use of her hands because of arthritis.

The palm is not very suitable for capillary studies because of the thick horny layer and the fact that the vessels run perpendicular to the cutaneous surface. Thus, only the end of the capillary loop can be seen as a red dot. In a normal palm a certain number of these dots can often be faintly seen arranged in regular rows following the cutaneous ridges. In our patients with palmar erythema the capillaries were easily seen and many more were visible (fig. 2) than in the normal palm. It has been suggested [3] that the color is the result of a thinned horny layer. Histologic reports do not confirm this opinion, and there is no gross evidence suggesting thinness or atrophy of the epidermis.

These observations would seem to indicate that there is capillary dilatation in all the palmar areas involved, plus a probable dilatation of the superficial arterial or venous plexus to give the underlying pink color. Such suppositions are consistent with the capillaroscopic and histologic observations of Mierowsky,[4] which are mentioned in another part of the paper.

No detailed report of the histologic findings in naevus araneus could be found in the literature. McCarthy [5] stated that the central vessel is an arteriole which divides into branching veins. McKenna [6] said that the central vessel may be either a venule or an arteriole. Biopsies were made by us of ordinary spider nevi from nonpregnant women for comparison.

Biopsy was made of one of the naevus-araneus-like lesions of a patient (case 11) about one month before delivery. The lesion, reconstructed from serial sections, seemed to consist chiefly of an arteriole branching from one of the arteries just within the subcutis. This vessel traversed a somewhat tortuous course to about the subpapillary layer of the cutis

3. Aguilera Maruri, C.: Erythème palmaire symétrique, syphilitique? Ann. de dermat. et syph. **10**:415 (May) 1939.

4. Mierowsky, L.: Krankheitsbild des Erythema palmo-plantare symmetricum hereditarium, Arch. f. Dermat. u. Syph. **168**:420, 1933.

5. McCarthy, L.: Histopathology of the Skin, St. Louis, C. V. Mosby Company, 1931.

6. McKenna, R. W.: Diseases of the Skin, ed. 4, Baltimore, William Wood & Company, 1937.

(fig. 3). Here it seemed to change directly into a vein of comparable size without intervening capillaries, which in turn divided into the network of smaller venules which form the gross spider-like appearance.

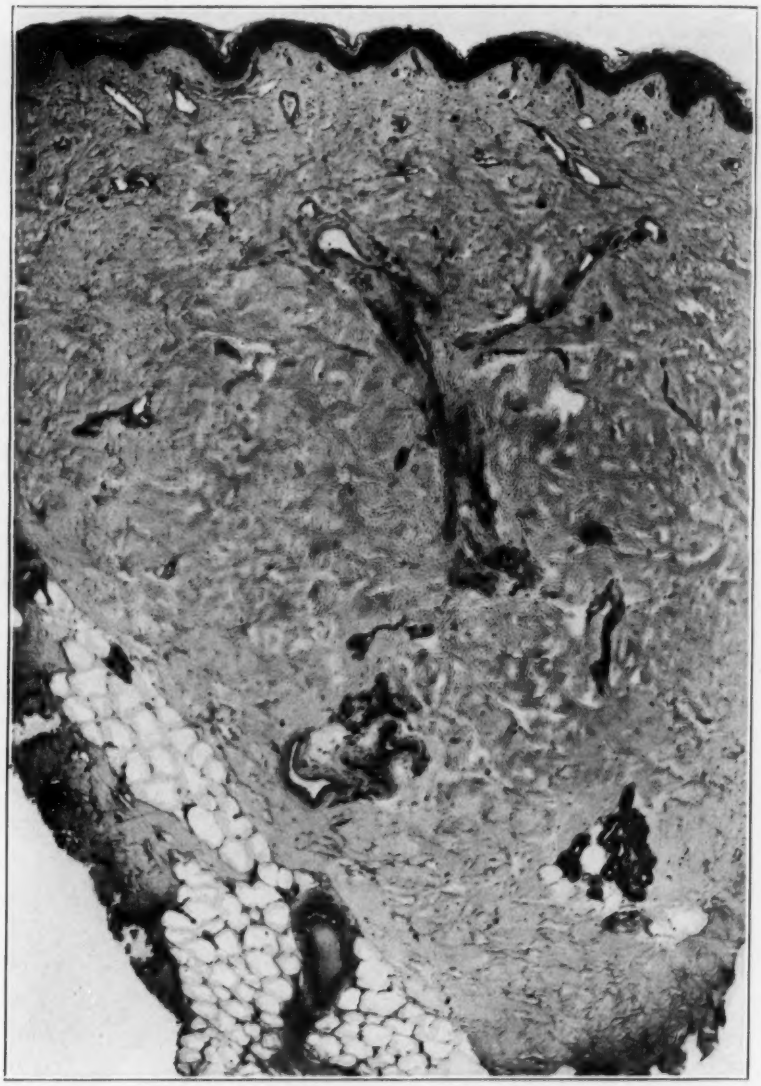

Fig. 3 (case 11).—Section of naevus-araneus-like lesion from forearm (low power; hemalum-erythrosin-saffron stain).

It had a muscular wall of about normal thickness for a vessel of its size (0.25 mm.) and was accompanied by a nerve whose fibers seemed to end in the vessel wall. An arteriole of such size is not normally seen so high in the cutis. Thus the lesion seems to consist of a small

arteriovenous anastomosis. A section of naevus araneus showed the same general structure, but the vessel walls were thicker. Detailed study will be reported in a subsequent publication.

REVIEW OF THE LITERATURE

The 2 original patients described by Lane [1] were men, one 51 years of age, in good health, and the other 69 years old, suffering from thromboangiitis obliterans. Each had had the condition as long as he could remember. Other members of the family were affected in both instances. The author suggested the possibility of some vasomotor paralysis but expressed the opinion that this was excluded by the fact that the involved vessels reacted in the usual manner to such stimuli as heat and cold. He also considered the possibility of a bilateral symmetric nevus, using the term in its broadest sense.

Ambler [7] presented a man aged 63 who had chronic gallbladder disease and had noticed redness of his palms for seven years. There was no familial history of the condition, and there were no subjective symptoms. Leukonychia totalis was also present. The Wassermann reaction of the blood serum was negative. It is an interesting observation that the temperature of the palms was 5 degrees (C.) higher than normal.

In Mierowsky's patient,[4] a man aged 38, the condition developed after his recovery from an abdominal wound. The author described the same capillaroscopic picture that was seen in our patients, i. e., a dilated superficial venous plexus and an increased number of open capillaries. Histologic examination showed no abnormality except dilatation of the superficial capillaries and some prominence of the endothelium. She considered the condition to be a hereditary anomaly, a genodermatosis.

Mierzecki [8] reported the case of a man aged 45 who had had the condition since birth. Several of his sisters and brothers also were affected.

Gottron [9] reported the cases of 2 men. In the first, aged 36, there was no evidence of a hereditary factor, and the patient had concretio cordis, which suggested to the author the possibility of a circulatory basis for the phenomenon. The second, aged 26, in whom the color was present at birth, was a student whose father showed the same type of change and who stated that at times he had a feeling of "spasm" in his hands.

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7. Ambler, J. V.: Erythema Palmare Hereditarium, Arch. Dermat. & Syph. **25**:1156 (June) 1932.

8. Mierzecki, R.: Erythema palmo-plantare hereditarium, Zentralbl. f. Haut- u. Geschlechtskr. **48**:280, 1934.

9. Gottron, H.: Erythema palmare hereditarium, Arch. f. Dermat. u. Syph. **172**:135, 1935.

Kerl [10] discussed the subject and presented 2 cases. A man of 45 came to the clinic because of hyperthyroidism following the taking of iodides. The palmar erythema had been noticed by the patient for only one month. One brother had similar palms. A second patient was inadequately described, but the erythema extended onto the dorsa of the hand and forearm. From the description given it is doubtful whether this case should be included in the erythema palmare group, although it was stated that the patient's father showed the same changes.

Bloemen [11] reported the case of a man aged 37 who had had palmar erythema for twenty-seven years. He also had tuberculous spondylitis and showed clubbing of the fingers. The family history was unknown.

Schmidt-La Baume [12] described the case of a man aged 49 who had had involvement of both palms and soles for fifteen years. No other changes were observed, except that the palms seemed drier than normal. The color was accentuated by the ingestion of alcohol, and the patient showed pronounced dermographism. There was a definite hereditary history in which the characteristic seems to have been present as an irregular dominant.

Aguilera Maruri [8] reported symmetric erythema of the ulnar sides of the palms of three years' duration in a man aged 54. The patient had tuberculosis and syphilis of long duration. The erythema gradually disappeared under antisyphilitic therapy. The author considered the condition due to a syphilitic lesion of the sympathetic nervous system or a sympathetic-endocrine imbalance of syphilitic origin. Histologic examination showed no abnormality.

A patient showing palmar erythema associated with pregnancy was recently reported by Feldman.[13] As in some of our cases, the erythema was mottled and had been present in previous pregnancies. No mention was made of the presence of naevus-araneus-like lesions or of a family history of the condition.

Telangiectases associated with pregnancy have been described repeatedly. Zeisler,[14] in 1922, presented a patient showing telangiectasis associated with syphilis and pregnancy.

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10. Kerl, W.: Erythema palmare hereditarium, Wien. med. Wchnschr. **86**:705 (June 27) 1936.

11. Bloemen, J. J.: Erythema palmare, Nederl. tijdschr. v. geneesk. **82**:1519, 1938; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **62**:406, 1939.

12. Schmidt-La Baume, F.: Zur Kenntnis des Erythema palmo-plantare symmetricum hereditarium, Dermat. Wchnschr. **109**:88 (Sept. 16) 1939.

13. Feldman, S.: Case for Diagnosis (Palmar Eruption Due to Endocrine Disturbances During Pregnancy), Arch. Dermat. & Syph. **39**:784 (April) 1939; Case for Diagnosis (Inflammatory Papules or Deep Telangiectasia Occurring During the Course of Pregnancy), ibid. **40**:1024 (Dec.) 1939.

14. Zeisler, E. P.: Telangiectasia Associated with Syphilis and Pregnancy, Arch. Dermat. & Syph. **5**:781 (June) 1922.

Konrad,[15] in 1925, described a patient with telangiectases on the forearms, neck and face which had appeared during the second month of pregnancy and which had nearly disappeared a few days after delivery. Aron,[16] in 1926, presented a patient who may have been the same one described by Konrad [15] and suggested an endocrine basis for the trouble. The patient had roentgenologic evidence and physical signs of pituitary tumor.

Urbach [17] presented 2 cases of telangiectasis of the naevus araneus type appearing in the fourth and in the sixth month of pregnancy and disappearing shortly after delivery.

Gougerot and Meyer,[18] in 1929, reported the case of a woman aged 25 who had telangiectases which developed during the fifth month of each of four pregnancies. These were in the form of spider nevi, chiefly on the hands, arms and neck. The mucous membranes were free, and there was no tendency to hemorrhage. The lesions faded in three to four months, leaving some cutaneous atrophy. Two sisters had had the same condition, and because of a history of syphilis in the family the authors considered it heredosyphilitic in nature. No abnormality of the palms was mentioned.

Pautrier and Ullmo [19] reported the case of a patient in whom after two normal pregnancies telangiectases developed chiefly on the right arm and on the neck with only a few on the left arm and the upper part of the chest during the third month of her third pregnancy. These lesions varied from small telangiectatic macules to definite spider nevi with elevated central puncta. The lesions were surrounded by anemic halos. No apparent cause was found. Biopsy was not performed, and the patient was not observed further. The condition in this patient seemed to correspond exactly to that in our case 10.

Another patient aged 32, whose case was reported by Forman,[20] showed telangiectases developing after the first month in the last eleven of twelve pregnancies. These eleven pregnancies were terminated by delivery of dead fetuses six weeks prematurely. The telangiectasis disappeared about five days after delivery.

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15. Konrad, E.: Zentralbl. f. Haut- u. Geschlechtskr. **17**:275, 1925.

16. Aron: Telangiectasien, Zentralbl. f. Haut- u. Geschlechtskr. **18**:755, 1926.

17. Urbach, E.: Essentielle Telangiectasien, Zentralbl. f. Haut- u. Geschlechtskr. **18**:339, 1925.

18. Gougerot, H., and Meyer, J.: Télangiectasies périodiques gravidiques et familiales, apparaissant et disparaissant avec la grossesse, Bull. Soc. franç. de dermat. et syph. **36**:1032, 1929.

19. Pautrier, L. M., and Ullmo, A.: Telangiectasie stellaire acquise chez une femme enceinte, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **38**:308, 1931.

20. Forman, L.: Telangiectasia Associated with Pregnancy, Proc. Roy. Soc. Med. **27**:723, 1934.

COMMENT

Erythema of the palms as seen and described by us seems to be a definite clinical entity, since the distribution, color and general appearance have been the same in all instances. However, in examining the histories for a possible common etiologic factor one is struck chiefly by the lack of regularity. There were 11 men and 9 women. The age of onset varied from birth to 56 years. Five of the women first had the redness during pregnancy, and 4 also had telangiectases on the arms, neck and face. In 1 of these cases there was a familial history; in 2 the condition had occurred in some of their preceding pregnancies but not in all, and in 2 it had not been present in preceding pregnancies. In our 5 remaining cases the redness had come on gradually at various ages and was associated with such diverse conditions as thyrotoxicosis, arthritis and leukoplakia. Two women had had children without noticing any change in the hands and without the development of telangiectases. Of the men, 3 were presumably in good health; in 1 the erythema followed an infected abdominal wound, and 1 had tuberculosis and syphilis. The others had chronic gallbladder disease, concretio cordis, hyperthyroidism, tuberculous spondylitis and pruritus ani.

Becker,[21] in his study of the telangiectases, divided them roughly into two groups, the hereditary and the acquired, although even with this broad subdivision it is difficult to classify certain cases. He divided causal factors in the latter group into neurogenic, toxic, mechanical and endocrine. Several factors may be combined in any one case.

Heredity is certainly most important etiologically in erythema palmare, since 11 of the total of 20 patients had a history of familial occurrence. However, the appearance of the erythema during pregnancy with and without known hereditary influences and the fact that in cases 1, 4, 8 and 9 and in 1 reported case [10] there was definite or suggestive evidence of thyroid dysfunction indicate that there may be an endocrine or hormonal factor.

The distribution of the erythema suggests some neurogenic factor, since it corresponds exactly with the special innervation of the palms, i. e., branches of the median and ulnar nerves which supply the skin of the palms and the dorsa of the terminal phalanges.

Mechanical influences probably play no part. The erythema is an active not a passive one, as evidenced by the color and the elevation of the cutaneous temperature, which was noticed by Ambler.[7] The fact that

21. Becker, S. W.: Generalized Telangiectasia, Arch. Dermat. & Syph. **14**:387 (Oct.) 1926; Further Studies on Generalized Telangiectasia, with Results of Treatment by Ultra-Violet Rays and Thorium-X, Acta dermat.-venereol. **8**:117, 1927.

the palms return to normal in some cases shows that the condition may be a functional and not necessarily an organic change.

There is no consistent association with a chronic toxic state. One patient was syphilitic; 1 had tuberculosis and syphilis, and 1 had chronic gallbladder disease. None of the pregnant women had toxemia of pregnancy or other complications, although Feldman's patient had had stillbirths in each of the pregnancies associated with the palmar erythema.

Thus, erythema palmare hereditarium is probably a functional genodermatosis. It may be present at birth or appear later in life, often in association with hormonal or endocrine disturbances which act on the underlying abnormal vascular or neurovascular system.

Syphilis,[22] sympathetic vasomotor dysfunction and hormonal or endocrine imbalance and hereditary factors [19] have all been suggested as possible causes of the telangiectasis occurring during pregnancy. Williams and Snell [23] observed the association of spider nevi with hepatic diseases and found that the cutaneous lesions sometimes precede any clinical evidence of hepatic damage. In none of our patients was there any evidence of syphilis or of liver dysfunction, although we observed an elderly man with severe hepatic disease who had telangiectases of the naevus araneus type. The patients in cases 9 and 10, as well as 4, showed evidences of thyroid dysfunction, as previously mentioned. No hereditary tendency was reported by any of our patients except when the condition was associated with erythema palmare. The usual etiologic explanation that spider nevi develop after minor traumas, such as mosquito bites and pinpricks, is not suggested at all in these patients. The significance of the biopsy findings is not clear. The development or hypertrophy of the central arteriole may be the result of some endocrine disturbance and may be related to the changes in the smooth muscle elsewhere in the body during pregnancy.

Pautrier [19] pointed out that the distribution of the lesions in his patient coincided with the area supplied by the brachial plexus but went no further in suggesting that the lesions were of nervous origin.

SUMMARY

Twenty cases of erythema palmare hereditarium, 9 presented by us and 11 collected from the literature, are reviewed. In 4 of our cases the condition appeared during pregnancy and was associated with the development of naevus-araneus-like lesions on the arms, face, neck and upper part of the chest. This complete clinical picture has not previously

22. Zeisler.[14] Pautrier and Ullmo.[19]

23. Williams, D. H., and Snell, A. M.: Pulsating Angioma (Generalized Telangiectasia) of the Skin Associated with Hepatic Disease, Arch. Int. Med. **62:** 872 (Nov.) 1938.

been described. Capillary studies usually showed a dilatation of the venous side of the capillary loops and the superficial venous plexus. In some patients both the redness of the palms and the telangiectases disappeared after delivery.

Erythema palmare hereditarium may be a functional genodermatosis which may be precipitated by toxic or hormonal influences.

The latter seem to be the chief causative factors in the associated telangiectases which often occur in pregnancy unaccompanied by redness of the palms and which show no hereditary tendency.

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COMBINED FUNGOUS INFECTIONS

REPORT OF SIX CASES WITH A REVIEW OF THIRTY-SIX CASES FROM THE LITERATURE

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The simultaneous presence of two or more pathogenic microorganisms in the same patient is not rare as far as bacteria are concerned. The symbiosis of streptococci and staphylococci, a mixed ulcer with bacilli of Ducrey and Spirochaeta pallida, tuberculosis and syphilis in the same patient, or even in the same granulomatous lesion, are examples of combined bacterial infections.

Several nonpathogenic fungi, molds or yeasts often grow together in cultures of the skin, scales, hairs or nails. The association of one pathogenic fungus with other nonpathogenic types is also common. A true combined mycotic infection with two or more different pathogenic species present in the same person is, however, rare, in spite of the frequent occurrence of fungous diseases due to various fungi. This fact has been noted by many observers.

Bodin,[1] who described a patient with trichophytosis and favus of the scalp, emphasized that instances of this condition were very rare. According to Mitchell,[2] "Sabouraud says that two pathogenic fungi are never found in the same person." Grütz [3] among many hundreds of observations did not observe a single case in which two different fungi were present. Karrenberg [4] stated that in spite of the theoretic possibility of a superinfection with a fungus in addition to an infection with a fungus of another species, such cases are seldom observed in practical work.

Fungi present in cases of combined infections may belong to different genera, such as Trichophyton, Achorion, Microsporon and Mon-

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From the Department of Dermatology and Syphilology of the New York University College of Medicine, Service of Dr. Frank C. Combes.

1. Bodin, E.: Coexistence de teignes faveuses et trichophytiques sur un même cuir chevelu, Ann. de dermat. et syph. **1**:327, 1910.

2. Mitchell, J. H.: Further Studies on Ringworm of the Hands and Feet, Arch. Dermat. & Syph. **5**:174 (Feb.) 1922.

3. Grütz, O.: Ueber Variabilität pathogener Hautpilze, Zentralbl. f. Bakt. (Abt. 1) **93**:268, 1924.

4. Karrenberg, C. L.: Gleichzeitige Infektion mit drei verschiedenen Trichophytonarten, Arch. f. Dermat. u. Syph. **154**:668, 1928.

ilia, or they may be species of the same genus, for instance, two different Trichophyta.

REPORT OF CASES

Six patients with combined fungous infections were observed at the dermatologic clinic of the New York University College of Medicine during the ten years from 1930 to 1940. In 1 the condition was a combination of trichophytosis and favus of the scalp. In the other 5

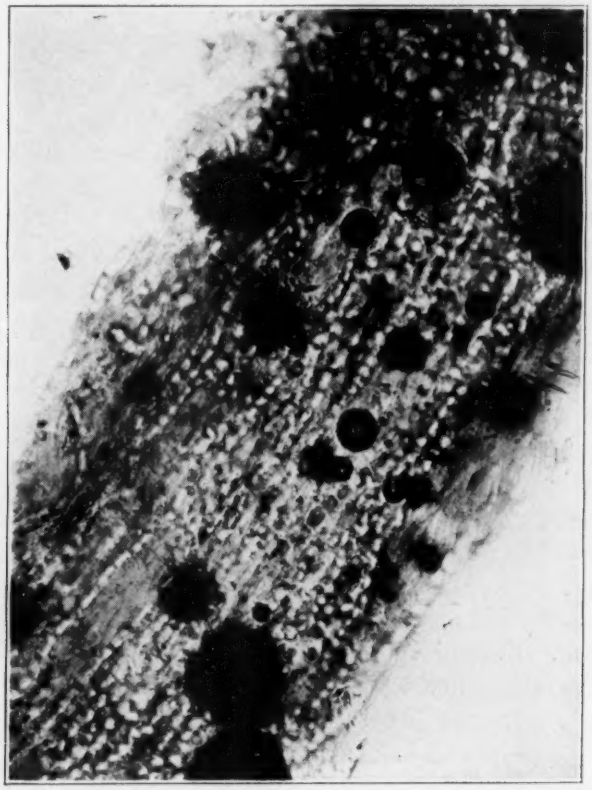

Fig. 1 (case 1).—A. schoenleinii in a hair from the scalp (potassium hydroxide preparation).

patients Epidermophyton and Monilia albicans were simultaneously present.

CASE 1.—*Trichophytosis and favus of the scalp.*

R. N., a white girl aged 15, born in the United States, gave a history of a disease of the scalp of eight years' duration.

On examination the scalp presented several irregular areas of erythema, scaling, atrophy and alopecia and numerous yellow scutula embedded in the epidermis

and pierced by hairs. The latter were dull and grayish and could be easily and painlessly epilated.

Clinical diagnosis of favus was corroborated by microscopic examination. In a fresh preparation made with 30 per cent of solution of potassium hydroxide, numerous air bubbles were seen on the surface of the hair, inside of which there were long septate and branched hyphae and chains of rectangular spores running parallel with the long axis of the hair (fig. 1). Its root contained numerous hyphae and polymorphous spores surrounding the hair shaft. The scutula consisted of a central dense mass of fungi without a definite structure and a border made up of hyphae radiating in all directions.

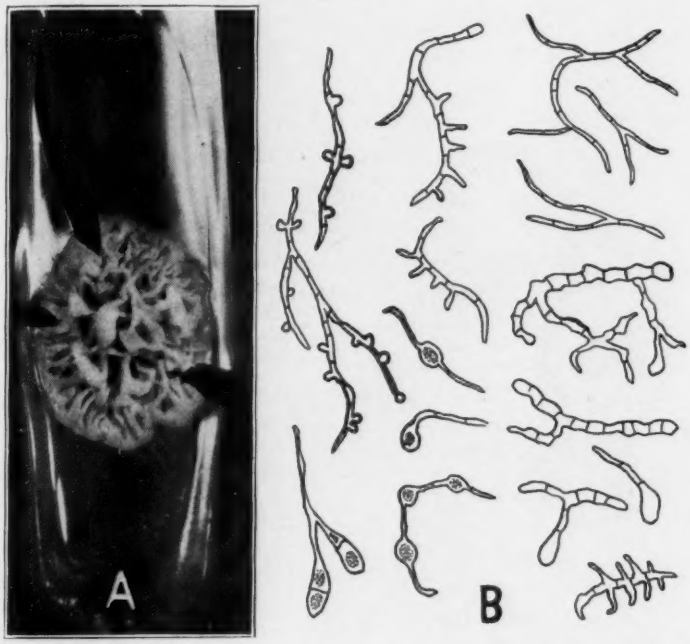

Fig. 2 (case 1).—A. schoenleinii. *A*, culture of organisms from the scalp. *B*, forms of mycelium and spores in a slide culture (drawing).

Cultures on Sabouraud's dextrose-peptone-agar were characteristic for Achorion schoenleinii. The growths were elevated, brownish, convoluted and waxy, extending deep into the medium, which showed several radial cracks (fig. 2 *A*). Slide cultures revealed polymorphous septate and branched hyphae with terminal knobs or short branches resembling horns or candlesticks, also pectinate bodies, chlamydospores, scanty lateral conidia and a few rudimentary spindles (fig. 2 *B*).

Roentgen ray epilation of the scalp was performed on June 13, 1939. Eight weeks later the scalp looked free from favus, and microscopic examination of hairs and scales from the formerly affected areas showed no organisms. However, new foci, different from favus, were noticed on both temporal regions of the scalp. They were small, ¼ inch (0.6 cm.), roundish areas with apparently

normal skin and hairs in the form of comedo-like black dots embedded in the epidermis.

Microscopic examination revealed short and curved fragments of hairs completely filled with closely packed globular spores, a picture of Trichophyton endothrix and different from one observed in favic hairs (fig. 3).

Cultures from these black dots gave Trichophyton violaceum. The central part of the colony was finely convoluted and the periphery flat with radial grooves. The surface was smooth and shiny. The violaceous color appeared

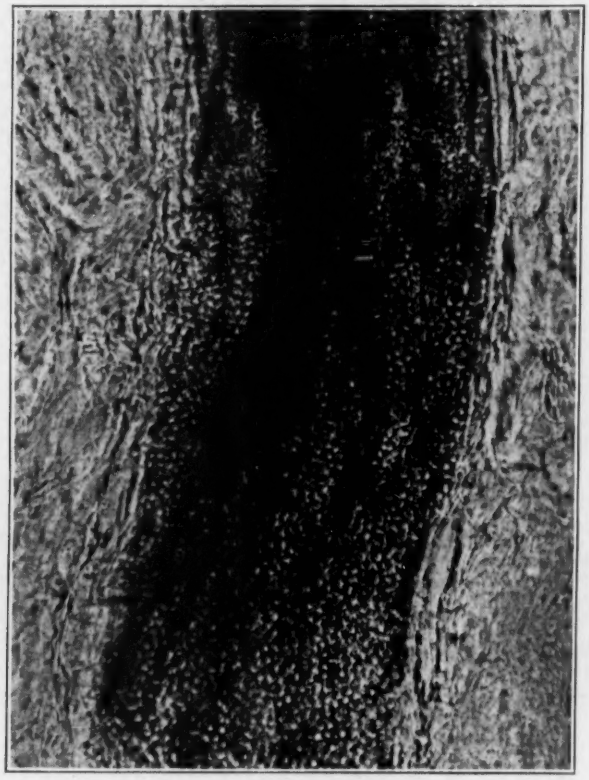

Fig. 3 (case 1).—T. violaceum in a hair from the scalp (potassium hydroxide preparation).

first in the center and later spread to the periphery and became almost black (fig. 4). Slide cultures showed only septate and branched hyphae with chlamydospores. No other forms of spores were found (fig. 5).

Ten weeks after the roentgen ray epilation an erythematosquamous focus was noticed on the occipital region of the scalp and Achorion was found microscopically. During the next four months the trichophytic foci with comedo-like hairs were continuously visible and Trichophyton was found repeatedly. Achorion was also found twice. Both trichophytosis and favus were present simultaneously on

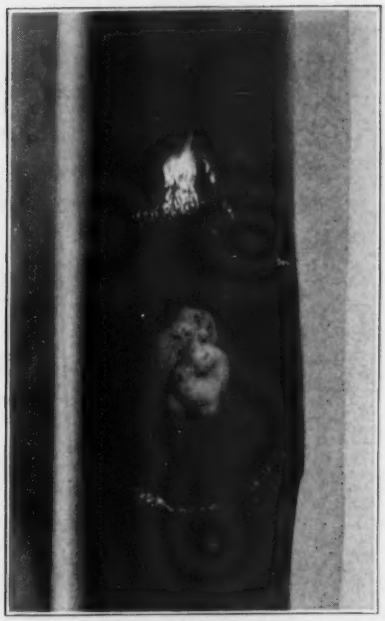

Fig. 4 (case 1).—Culture of T. violaceum from the scalp.

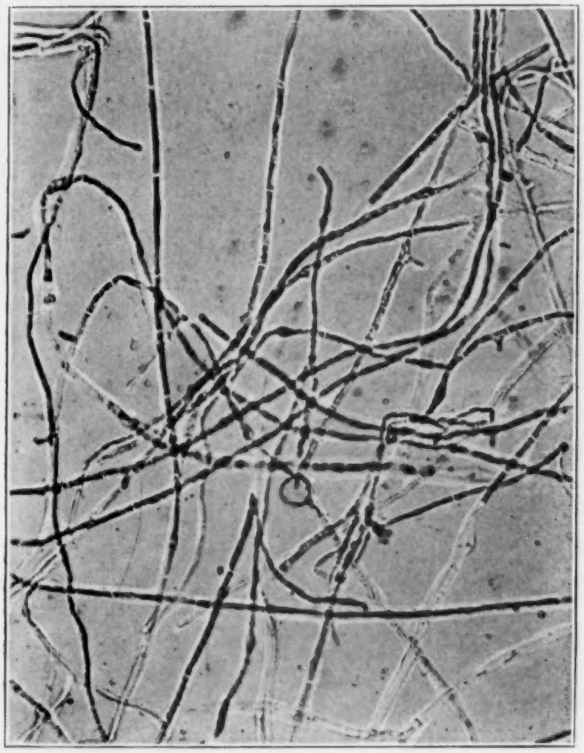

Fig. 5 (case 1).—T. violaceum: mycelium and chlamydospores in a slide culture.

the patient's scalp. At the end of December 1939, six and one-half months after roentgen ray epilation, nothing suggestive of favus was found, but trichophytic foci persisted and microscopically showed Trichophyton.

Case 2.—*M. albicans and Epidermophyton rubrum.*

R. N., a white man aged 60, a tailor, presented an extensive mycosis of two years' duration. In the second, third and fourth finger webs of both hands there were interdigital erosions. On the right palm and on both soles there were erythematosquamous patches. All the finger nails of the right hand, four finger nails of the left hand and several toe nails showed irregularities, fissures, yellowish-greenish discoloration and subungual hyperkeratosis (fig. 6). The toe webs of both feet were macerated. Both groins showed areas of intertrigo. In both

Fig. 6 (case 2).—Erosio interdigitalis due to a Monilia and onychomycosis due to an Epidermophyton.

axillas there were vesicular and erythematosquamous patches spreading to the flanks and to the back.

Eight samples of cutaneous material taken separately from various lesions showed fungi on microscopic examination. Those from the finger webs and the groins showed the Monilia type: a network of fine filaments and clusters of small roundish and ovoid yeastlike budding spores (fig. 7). The other six preparations, of material from the right palm, toe webs, soles, axillas, finger nails and toe nails, contained the Epidermophyton type: coarse filaments and chains of large spores (fig. 8).

Cultures were obtained from only three samples of the cutaneous material and corroborated the presence of two different parasites. The material from the

Fig. 7 (case 2).—M. albicans in the scrapings from erosio interdigitalis (potassium hydroxide preparation).

Fig. 8 (case 2).—E. rubrum in the scrapings from the axilla.

axillas gave E. rubrum, and that from the groins produced in four tubes twenty-eight pure colonies of M. albicans. The material from the finger webs showed in three tubes sixteen colonies of the same Monilia.

In the following 4 cases there was an association of M. albicans with Epidermophyton interdigitale.

CASE 3.—F. K., a white man aged 35, a factory worker, had had macerated toe webs for one year and presented vesicles on the soles of more recent origin. A microscopic preparation of material from the toe webs of the right foot showed a mixture of Epidermophyton and Monilia: long hyphae, chains of large polymorphous spores and also clusters of small yeastlike budding spores. A preparation of material from a vesicle on the right sole contained only the yeastlike elements. Cultures of material from the toes gave in three tubes twelve colonies of M. albicans, and material from the soles yielded E. interdigitale. Both fungi were evidently present in both locations.

CASE 4.—S. H., a white woman aged 40, a housewife, complained of itching in the toe webs of three weeks' duration. Examination revealed erythema, maceration and fissures in the toe webs of both feet. All the toe nails, especially those of the great toes, were irregular, yellowish, dull and fissured and showed subungual hyperkeratosis. The free borders of the nails were mostly affected. The changes of the toe nails were not noticed by the patient. Microscopic preparations of material from the toes and the toe nails showed only the Epidermophyton type of fungi. The material from the toe nails showed E. interdigitale and from the toe webs M. albicans.

CASE 5.—D. F., a white man aged 31, a vendor of newspapers, came to the clinic complaining of itching in the toe webs of one month's duration. The toe webs of both feet were macerated. Microscopic examination revealed fungi of the Epidermophyton type. Cultures planted in four tubes produced eighteen colonies of M. albicans and two colonies of E. interdigitale.

CASE 6.—M. C., a white man aged 58, a laborer, gave a history of an itchy eruption on the feet of three to four years' duration. The reaction to a trichophytin test was positive. The toe webs of both feet were dry, scaly and hyperkeratotic. Microscopically a mixture of Epidermophyton and Monilia was found. There were coarse and thick hyphae, chains of large polymorphous spores and also groups of closely packed small round and ovoid yeastlike spores, many of them budding. Cultures planted in five tubes produced thirty colonies of M. albicans and three colonies of E. interdigitale (fig. 9).

Cultures of Monilia isolated from lesions in the last 5 cases and grown on Sabouraud's dextrose-peptone-agar medium were identical, morphologically. Colonies two to three months old were yeastlike, pasty and of creamy color, with a moist, shiny surface and a honeycombed or

convoluted center. Transillumination revealed a mass of submerged growth penetrating deep into the medium and radiating in all directions on the periphery. Microscopic preparation of the surface layer of the culture showed only yeastlike budding cells. Characteristic forms were observed directly through the wall of the tube on the periphery of the colony. Another suitable method consisted of cutting out a portion of the medium with the submerged growth and crushing it between the slide and a cover glass in a drop of water or of lacto-phenol-blue (lactic acid, phenol crystal and distilled water, 20 cc. of each; glycerin, 40 cc., and aniline blue, 0.05 cc.). The latter preparation could be preserved by sealing it with asphalt varnish.

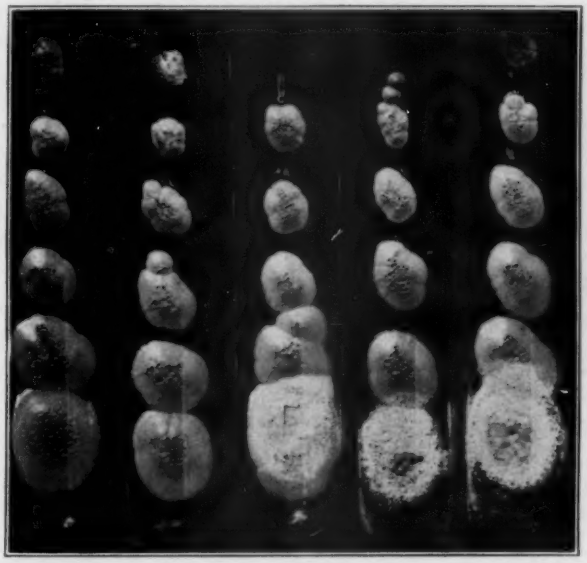

Fig. 9 (case 6).—Cultures from the toe webs showing thirty colonies of M. albicans and three superimposed colonies of E. interdigitale (lowermost in the last three tubes).

Microscopically, cultures of M. albicans showed well formed septate and branched hyphae and a great number of globular and ovoid yeast-like spores produced at intervals from the hyphae, often in spherical clusters. Numerous chlamydospores, large cells with heavy membrane, were also seen. Stab inoculations in tubes with gelatin produced a characteristic growth of treelike branched filaments radiating from the line of the stab. Fermentation tests with various carbohydrates were made with cultures from lesions in cases 2, 3 and 4, the results of which are shown in table 1.

In spite of the identical gross and microscopic appearance of the four cultures tested, their biochemical properties were not the same. The differences could be noted even between two Moniliae obtained from the finger webs and the groins of the same patient (case 2).

Comparison of microscopic and cultural results in cases 3, 4 and 5 reveals some discrepancies. The microscope may show only one type of fungi, Epidermophyton or Monilia, while the cultures give the other type or both of them. The reverse situation also occurs when the microscope shows both types of fungi while the cultures produce only one of them. Such contradictions are more apparent than real and will be analyzed in another section (Comment) of the paper.

REVIEW OF THE LITERATURE

The literature on combined fungous infections is scanty. The review of original articles on mycologic subjects, abstracts from cur-

TABLE 1.—*Results of Fermentation Tests with Cultures of Moniliae in Various Carbohydrates*

Case	Site of Lesions	Dextrose	Levulose	Maltose	Lactose	Galactose	Arabinose	Raffinose	Saccharose	Dextrin	Inulin	Mannite	Glycerin
2	Finger webs.....	GA	A	A	0	A	0	0	A	A	A	0	0
2	Groins.....	GA	GA	GA	0	GA	0	0	A	A	GA	0	0
3	Toes.....	GA	GA	GA	0	0	—	—	GA	0	0	—	—
4	Toes.....	GA	GA	GA	0	GA	0	0	GA	A	A	A	0

* The signs in the table have the following meanings: G, gas; A, acid; 0, no changes, and —, not done.

rent literature and transactions of various societies published in forty-one volumes of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY over a period of twenty years, from 1920 to 1940, revealed only 9 such cases. One of them (case 2 in my series) was presented by Dr. Howard Fox [5] at the meeting of the New York Dermatological Society on Jan. 26, 1932.

Altogether I found in the available literature 36 cases of combined fungous infections, which are briefly described.

Aubert [6] described 2 girls aged 10 and 16 years with favus of the scalp, who also showed short broken hairs embedded in the epidermis in the form of comedo-like black dots which, on microscopic exami-

5. Fox, H.: Extensive Infection with Mold and Yeastlike Organisms, Arch. Dermat. & Syph. **26**:539 (Sept.) 1932.

6. Aubert: Deux observations d'herpes tonsurant survenant chez des malades en cours de traitement pour un favus, Lyon méd. **22**:583, 1876.

nation, were completely filled with large roundish fungus spores. Cultures were not made, but the author considered that the black dots contained a Trichophyton as a superinfection on the preexisting favus. Sabouraud [7] mentioned Aubert's cases and also interpreted them as instances of combined infection with favus and trichophytosis.

Bodin [1] observed a 14 year old girl who had one large and several smaller lesions of favus with atrophy, alopecia and characteristically changed hairs on the vertex of the scalp. A. schoenleinii was found microscopically. Simultaneously, there were present on the lateral and posterior parts of the scalp about ten small roundish foci, 2 to 3 cm. in diameter, with hairs in the form of black dots, which, on microscopic examination, contained T. endothrix. Cultures were not made, but the clinical and microscopic data were such that the case was considered one of a combined infection with favus and trichophytosis.

Brault and Viguier [8] mentioned a patient with favus and trichophytosis of the scalp from whom they obtained cultures of A. schoenleinii and T. violaceum.

Lombardo [9] reported 3 cases in children in the same family, all of whom had simultaneously favus and trichophytosis. Cultures gave A. schoenleinii and two different Trichophyta whose species were not mentioned.

Sabouraud [7] saw combined infections with Trichophyton crateriforme and a Microsporon in children.

Finkelstein and Sigalova [10] observed a patient in whom T. violaceum and a Microsporon (species ?) were present simultaneously.

Bresciani [11] reported the case of a man aged 32 who had an onychomycosis of several finger nails and erythematosquamous and vesicular lesions on the beard and on the back of the neck with involvement of hairs. Cultures from the finger nails gave Microsporon audouini; from the beard and neck, T. violaceum.

Hartman [12] described a man aged 33 with tinea circinata of the abdomen, pubis and right thigh. Cultures gave two different fungi, Trichophyton gypseum and Cephalosporium.

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7. Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910.

8. Brault, J., and Viguier, A.: Les champignons de teignes rencontrées à Alger, Ann. de dermat. et syph. **6**:169, 1916.

9. Lombardo, C., in discussion on Oro, A.: Sul granuloma tricofitico del Majocchi, Gior. ital. di dermat. e sif. **67**:261, 1926.

10. Finkelstein, J., and Sigalova, E.: Gribkovie Zabolevania, Leningrad, Sanprosvet Guvzdrava, 1925.

11. Bresciani, J.: Contributio casistico allo studio delle onicomicosi rare, onicomicosi da Microsporum audouini, Gior. ital. di dermat. e sif. **66**:1085, 1925.

12. Hartman, E.: Ueber ein gemeinsames Vorkommen von Cephalosporium und Trichophyton gypseum, Dermat. Wchnschr. **82**:565, 1926.

Lewis and Hopper [13] described a patient with tinea versicolor of the chest and erythrasma in the axilla, a combined infection with Microsporon furfur and Microsporon minutissimum.

Weidman [14] observed a case of tinea versicolor and erythrasma in a white man aged 24. M. furfur was found microscopically in the patches on the shoulders and around the axillas. M. minutissimum was found in the groins. The lesions in the axillas contained both fungi. From the history of the case, the author assumed that erythrasma was the primary disease.

Hazel and Lamb [15] described a 23 year old woman with an involvement of the skin and of the mucous membranes of the tongue and mouth. The lesions in the mouth had been present for seven or eight years and the cutaneous changes for three or four months. On the neck, on the arms and on the abdomen there were irregular, sharply marginated erythematous plaques, from 1 to 3 cm. in diameter, with elevated borders and scaly centers. The finger nails and toe nails were rough, elevated, opaque and brittle. The tongue was deeply fissured and covered with a grayish white heavy moist coating. Cultures from the tongue produced M. albicans, and different sites of the skin and hair yielded Microsporon lanosum.

Ayres [16] demonstrated a woman with perlèche, dermatophytosis in the toe webs, onychomycosis of both thumb nails, one of which had been affected for thirty years, and ringworm of the scalp, with short broken hairs in the form of black dots, in which large spores were found microscopically. Cultures from the mouth gave M. albicans; cultures from the toe webs and from a thumb nail gave E. interdigitale. Unfortunately, the fungus growing from the hairs could not be identified. The clinical picture and the microscopic structure suggested T. endothrix. If this fungus had been cultured the condition would have been a combined infection with three different parasites.

Lane [17] demonstrated a woman aged 28 with dermatophytosis of the toe webs and a generalized eruption on the chest, back, buttocks and thighs consisting of polycyclic areas with red raised borders. Cultures from the toes revealed M. albicans, and cultures from the body, Trichophyton purpureum.

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13. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc., 1939, p. 149.

14. Weidman, F.: Erythrasma and Tinea Versicolor, Arch. Dermat. & Syph. **10**:236 (Aug.) 1924.

15. Hazel, O. G., and Lamb, J. H.: A Generalized Skin Eruption with Gastro-Intestinal Involvement Due to Two Different Species of Fungi, J. Oklahoma M. A. **27**:395 (Nov.) 1934.

16. Ayres, S.: Tinea Capitis in an Adult with Scar-Producing Alopecia, Arch. Dermat. & Syph. **23**:543 (March) 1933.

17. Lane, C. G.: Tinea Corporis (Trichophyton Purpureum): Moniliasis of Feet, Arch. Dermat. & Syph. **40**:119 (July) 1939.

Castellani [18] noted that pruritus vulvae or pruritus ani and intertrigo in the finger webs or groins may be due to a mixed infection with Epidermophyton and yeastlike parasites of various genera, for instance, Monilia.

Tschernogubow and I [19] described 8 patients with combined fungous infections observed in Russia. In 7 both mycoses were localized on the scalp (6 presented a combination of trichophytosis and favus, and 1 had microsporosis and favus). One patient had trichophytosis of the scalp and microsporosis of the glabrous skin. A brief description of the cases follows.

CASE 1.—L. C., a girl aged 7 years, had one large focus of favus on the top of the scalp, from which A. schoenleinii was cultured. Roentgen ray epilation was unsuccessful, and the patient remained in the hospital. Three months later new small lesions with short broken hairs were noticed beside the old focus of favus. Cultures from these hairs produced T. violaceum. The condition was apparently a superinfection with trichophytosis added to the already present favus.

CASE 2.—W. D., a boy aged 12 years, had a few foci of favus with atrophy on the vertex of the scalp. A. schoenleinii was grown in cultures. In the same part of the scalp and also in the occipital and temporal regions there were numerous small erythematosquamous lesions with short broken hairs, some in the form of black dots, from which T. crateriforme was cultured.

CASE 3.—P. G., a boy aged 15 years, presented one large focus of favus with atrophy and alopecia on the vertex of the scalp. A. schoenleinii was found in cultures. Besides, there were present in the occipital and temporal areas of the scalp numerous small lesions with short broken hairs, from which T. crateriforme was isolated.

CASE 4.—M. K., a boy aged 8 years, had numerous foci of favus on the vertex of the scalp. A. schoenleinii was cultured. There were also several small lesions with small broken hairs in the occipital and temporal areas which yielded T. violaceum in cultures.

CASE 5.—B. A., a girl aged 13 years, presented several large foci of favus on the vertex of the scalp and in the right temporal region. A. schoenleinii was isolated in cultures. Numerous lesions with short broken hairs were also found all over the scalp, from which T. violaceum was grown.

CASE 6.—W. L., a boy aged 12 years, had a few lesions of favus on the vertex of the scalp. Cultures revealed A. schoenleinii. Numerous small foci with short broken hairs were also present all over the scalp. From these hairs cultures of T. crateriforme were obtained.

CASE 7.—A. J., a girl aged 11 years, had favus, probably of long duration, with atrophy and alopecia on the vertex of the scalp. A. schoenleinii was grown

18. Castellani, A.: Fungi and Fungous Diseases, Chicago, American Medical Association, 1928, pp. 139, 141, 155-158, 164, 166, 168 and 170.

19. Tschernogubow, N., and Muskatblit, E.: Klinische Beobachtungen über die Immunität bei oberflächlichen Pilzerkrankungen der behaarten Kopfhaut, Arch. f. Dermat. u. Syph. **159**:46, 1929.

in cultures. The patient also presented in the occipital and right temporal regions two small foci, evidently of recent origin, with short broken hairs, from which M. lanosum was isolated.

CASE 8.—W. K., a boy aged 13 years, had numerous small foci with short broken hairs all over the scalp. T. violaceum was cultured. On the left cheek there was one small lesion of tinea circinata, evidently of recent origin, which gave cultures of M. lanosum.

The literature cited demonstrated infection with two fungi of different genera.

Bresciani [11] reported a rare combination of three fungi of different genera. The patient, a 40 year old man, had a generalized mycosis of the forearms, neck, back, beard and nails due to T. violaceum. In addition, there were also lesions of tinea versicolor and erythrasma. M. furfur and M. minutissimum were found microscopcially.

Cases are on record in which two or even three different species of the same genus were simultaneously present in the patient's skin.

Barbaglia [20] obtained cultures of T. violaceum and Trichophyton cerebriforme from the same scalp.

Artom [21] described a woman aged 48 with a generalized erythemato-squamous eruption from which Trichophyton glabrum was cultured. The patient presented also several large granulomatous tumors which gave cultures of Trichophyton faviforme.

Mitchell [2] found two different Epidermophyta in a patient. From a lesion on the thigh Epidermophyton inguinale was obtained and from the toes the "white" fungus (apparently E. interdigitale).

Karrenberg [22] isolated in a case of tinea capitis in a young boy two different fungi, of which he identified one as E. inguinale and the other as a fungus similar to E. rubrum. Microscopically endothrix growth was demonstrated in the hairs. This case was remarkable as an instance not only of a combined infection with two fungi on the scalp but also of an Epidermophyton involving the hairs.

Tschernogubow and I [19] described 7 patients, 5 girls and 2 boys, with ringworm of the scalp. Cultures showed in each case two different Trichophyta, namely, T. violaceum and T. crateriforme. Four children presented numerous small foci all over the scalp, and 3 had only a few lesions. Inflammatory reaction was slight. The affected hairs appeared in 3 patients as black dots, in 4 others as short broken stumps. None of the children showed a combination of foci of different clinical appearance which could suggest a mixed infection.

20: Barbaglia, V.: I tricofiti della provincia di Sassari, Gior. ital. di mal. ven. **55**:911, 1914.

21. Artom, M.: Imponenti formazioni tumorali profonde da trichophyton in tricofizia universale, Gior. ital. di dermat. e sif. **74**:563, 1933.

22. Karrenberg, C. L.: The Present State of Epidermophytosis in Europe, Arch. Dermat. & Syph. **17**:519 (April) 1928.

Karrenberg [4] reported on a patient with three different Trichophyta. A girl aged 8 years had an erythematous and infiltrated lesion on the back of the left hand. A few weeks later an acute inflammatory focus with short broken hairs developed on the scalp. Cultures from the hand produced T. faviforme; cultures from the scalp, T. cerebriforme and Trichophyton niveum.

SUMMARY OF OBSERVATIONS IN MY CASES AND IN THOSE REPORTED IN THE LITERATURE

Sex and Age.—The sex was indicated for 34 of 42 patients. Sixteen were males, and 18 were females. The age was stated for 25 patients;

TABLE 2.—*The Location of Lesions from Which Fungi Were Obtained*

Location	Number of Cases
Scalp only	21
Glabrous skin only	8
Scalp and glabrous skin	3
Glabrous skin and nails	2
Glabrous skin, nails and beard	2
Scalp, glabrous skin, nails and mouth	1
Total	37

TABLE 3.—*Frequency of Involvement of Areas of Skin by Fungous Infections*

Area Involved	Number of Cases
Scalp	25
Glabrous skin	16
Nails	5
Beard	2
Mouth	1

11 were referred to as children, and for 6 no age was given. In the group below 16 years of age are included the children. The patients can then be divided into the following age groups: from 7 to 16 years, 24 patients; from 23 to 35 years, 7 patients, and from 40 to 60 years, 5 patients.

Location of the Lesions.—Table 2 shows the location of the lesions from which different fungi were obtained. Data are available in 37 cases.

Table 3 shows the relative frequency of involvement of different areas of the skin in the 37 cases of combined fungous infections. Twenty-one of the 25 patients with involvement of the scalp were from 7 to 16 years old; 1 was 48 years old. In 3 cases the age was not given.

Proximity of Foci of Different Mycoses.—In many cases of combined infections the foci produced by different fungi are widely separated. In

1 of Bresciani's cases M. audouini was found in the finger nails and T. violaceum on the beard and neck. In Ayres' case M. albicans was present in the corners of the mouth and E. interdigitale on the toes and a thumb nail. In Lane's case M. albicans was cultured from the toe webs and T. purpureum from the chest, back, buttocks and thighs. In 1 of my cases M. albicans was found in the finger webs and groins and E. rubrum in the axillas.

In some instances the lesions due to different fungi are in close proximity, for instance, in cases of trichophytosis and favus on the scalp. But even then the two mycoses are localized in separated areas. Favic and trichophytic hairs are not intermixed in the same focus, nor are both fungi present in the same hairs.

Finally, there are cases in which different fungi are found in the same lesion, true mixed infections. Karrenberg's patient had two different Trichophyta isolated from a single focus on the scalp; in Weidman's

TABLE 4.—*Fungi Found in Forty-Two Cases of Combined Infections*

Fungus	Number of Cases
Trychophyton	40
Achorion	15
Epidermophyton	9
Monilia	8
Microsporon	5
M. furfur	3
M. minutissimum	3
Cephalosporium	1

case M. furfur and M. minutissimum were found in the same patches, and in 2 of my cases M. albicans and E. interdigitale were cultured from the same toe webs. In such cases it is impossible to say which part of the lesion is due to one fungus and which to the other. Both parasites are present in a state of a real symbiosis in the same area of the skin.

Genera and Species of Fungi.—The genera and species of the fungi were in the majority of cases determined by cultures. Table 4 gives a summary of fungi found in 42 cases of combined infections. Doubtful organisms, like "white fungus" (Mitchell) and "a fungus similar to E. rubrum" (Karrenberg), were not included. The species called by some E. rubrum and by others T. purpureum is included in the Epidermophyton group because it is found, with rare exceptions, only in the glabrous skin or nails. The species of the genus Trichophyton observed in 40 cases are given in table 5.

The prevalence of endothrix (28 out of 40) Trichophyta may not be purely accidental. These fungi are human types. They usually cause noninflammatory conditions, do not produce active sensitization, do not stimulate immunity and therefore cannot prevent another fungus

from invading the skin later. Trichophyta of the neoendothrix and ectothrix subdivisions are of animal origin, cause inflammatory lesions, induce sensitization and immunization and thereby protect the skin from a superinfection with another fungus.

Fungi of the genus Achorion were found in 15 cases. In 12 the cultures revealed the species A. schoenleinii. In 3 cases (Aubert and Bodin) cultures were not made, but it is highly probable that the species was the same, as it is the only usual cause of favus of the scalp in man.

TABLE 5.—*The Species of Trichophyton Found in Forty Cases*

Trichophyton		Number of Cases
Endothrix	violaceum	17
	crateriforme	10
	glabrum	1
Neoendothrix	cerebriforme	2
Ectothrix	faviforme	2
	gypseum	1
	niveum	1
Species unknown (?)		6
Total		40

TABLE 6.—*Combinations of Organisms in Patients with Double Infections*

Fungi	Number of Cases
Trichophyton and Achorion	14
Two Trichophyta	9
Monilia and Epidermophyton	7
Trichophyton and Microsporon	3
M. furfur and M. minutissimum	2
Trichophyton and Cephalosporium	1
Microsporon and Achorion	1
Microsporon and Monilia	1
Epidermophyton and unknown species	2
Total	40

Fungi of the genus Epidermophyton were isolated in 9 cases, in 5 of which the species was E. interdigitale, in 2 E. rubrum and in 2 E. inguinale.

Monilia, found in 8 patients, was referred to the species M. albicans.

Microspora were isolated in 5 cases; in 3 the species was M. lanosum, and in 1, M. audouini; in 1 it was not stated.

Combinations of Fungi.—Forty of 42 patients had a double infection, and 2 had a triple one. The last 2 were a patient with T. violaceum, M. furfur and M. minutissimum and 1 with three Trichophyta, T. cerebriforme, T. faviforme and T. niveum. The combinations of organisms in the 40 patients with two different fungi are given in table 6.

The association of Trichophyton and Achorion was the most frequent. Ten of 14 patients with this combination were from 7 to 16 years of age; 3 were reported as children, belonging probably to the same age group, and for 1 the age was not stated. Four were males; 6 were females, and the sex of 4 was not indicated. In 11 patients, both mycoses were localized on the scalp, and in 3 the location was not given but in all probability was the same. Favus presented a typical appearance in all those cases in which the clinical description was given. Trichophytosis was mostly in the form of small lesions of a noninflammatory type with short broken hairs, in some cases as black dots. Cultures from 5 patients showed T. violaceum and from 3 T. crateriforme; in 6 cases the species remained unknown.

A combination of two different Trichophyta occurred in 9 patients, seven were from 8 to 14 years of age, and 1 was 48 years old; the age of 1 was not stated. In 1 case the clinical picture was not given. In another there were erythematosquamous lesions and large tumor-like granulomas on the scalp and the glabrous skin. The remaining 7 patients presented on the scalp small foci with short broken hairs and insignificant inflammatory reactions. The cultures from 7 patients showed a combination of T. violaceum and T. crateriforme; from 1 patient, T. violaceum and T. cerebriforme, and from 1 patient, T. glabrum and T. faviforme.

Association of Monilia and Epidermophyton was observed in 7 patients from 28 to 60 years of age. In 2 of them both fungi were isolated from the same lesions; in 5 they were located separately. Monilia was found mostly in the toe webs (5 patients) but also in the finger webs, groins and corners of the mouth. Epidermophyton was cultured from the toe webs, toe nails, thumb nails, soles and axilla, and in 1 case the eruption was generalized. It is of interest that the Monilia-Epidermophyton combination was seen only in adults, while the Trichophyton-Achorion combination occurred in children.

Association of a Trichophyton with a Microsporon was found in 3 patients. T. violaceum was cultured from all. The Microsporon was in 1 case M. audouini and in 1 M. lanosum, and in 1 case the species was not stated.

Although the name Microsporon has been given to both M. furfur, of tinea versicolor, and M. minutissimum, of erythrasma, the organisms are entirely unrelated. They do not belong to the same genus. Therefore, they are mentioned as two independent species, separate from each other and from all other fungi discussed in the paper. They cannot be included under the genus Microsporon (of ringworm), which includes M. audouini, M. lanosum and others. The combined infection with M. furfur and M. minutissimum is mentioned as such and not as one with two Microspora because the latter term would suggest two different species of the same genus Microsporon (of ringworm).

The use of the name Microsporon for fungi of tinea versicolor and of erythrasma is a misnomer from the point of view of correct mycologic terminology. The generic name Microsporon should be reserved exclusively for fungi related to ringworm (M. audouini, M. lanosum and others). The fungus of tinea versicolor should be called Malassezia furfur and the fungus of erythrasma Actinomyces minutissimum. These names, however, are seldom given, and the old ones, M. furfur and M. minutissimum, are traditionally used.

Succession of Mycoses.—The knowledge of which fungus was the first and which the second invader is important from the immunologic viewpoint. The necessary data are, however, usually lacking. The problem cannot be solved when two different fungi are found in the same lesion. Even in cases with separate foci the history is unreliable, as the changes of the skin may have escaped the patient's attention for a long time.

In 1 case it was probable that T. violaceum was the first to involve the scalp and was followed by a M. lanosum infection of the face. In another case the patient had an inflammatory lesion on the hand due to T. faviforme, an animal species with high sensitizing power. Despite this, two other Trichophyta (T. cerebriforme and T. niveum) attacked the scalp later.

In 3 patients A. schoenleinii was probably the first invader of the scalp, followed by a superinfection with a Trichophyton or a Microsporon. In 1 case an E. interdigitale infection of a thumb nail existed for thirty years and then perlèche due to Monilia developed. In another case onychomycosis of the toe nails caused by E. interdigitale was present for one year when a moniliasis of the toe webs supervened.

In 3 cases in which M. lanosum was isolated it was the second invader preceded by A. schoenleinii, T. violaceum and Monilia. No instances were found in which M. lanosum as the first infection was followed by a second fungous infection. This fact suggests that M. lanosum, an animal species capable of producing considerable inflammatory reaction and allergic transformation, may possess a certain immunizing power protecting its host from a superinfection with another fungus.

M. albicans was the first invader in 2 patients. In 1 patient moniliasis of the tongue existed for several years before M. lanosum attacked the glabrous skin, the hair and possibly the nails. In another patient moniliasis of the toe webs was followed by an E. rubrum infection of the trunk and thighs. Monilia belongs to a class of fungi apart from other genera causing ringworm and favus. They usually produce superficial lesions of long duration and little immunologic response which will hardly prevent an invasion with other fungi. Such combined infections will probably be found more often if cultures are secured from all patients and the material is taken separately from various lesions.

M. furfur and M. minutissimum were found together in 3 cases. In one of them, erythrasma was the first infection. Both fungi lead a saprophytic existence in the skin, cause little or no reaction and obviously do not create any immunity. Tinea versicolor and erythrasma are frequently overlooked because of insignificant symptoms and signs. Closer attention and microscopic examination would probably reveal many more cases of these conditions present simultaneously, or either or both present in combination with other mycoses. In 1 patient both were found together with lesions due to T. violaceum, forming a triple fungous infection.

DIAGNOSIS OF COMBINED FUNGOUS INFECTIONS

The recognition of two different fungi by clinical observation alone without a laboratory examination is possible only when the two parasites are located separately and produce characteristic pictures. When the scalp is affected favus can be differentiated from ringworm. The differentiation of trichophytosis and microsporosis on the scalp is often impossible.

When the glabrous skin or nails are affected, the identification of the fungus from the clinical picture is, in the majority of cases, impossible, as many species may produce similar manifestations.

Microscopic examination reveals the presence of two different organisms if hairs are involved. Then it is possible to recognize Trichophyton, Microsporon and Acorion. However, they, and also the Epidermophyton, look very much alike in the scrapings from the glabrous skin and nails in which the diagnosis not only of the species but even of the genus is impossible.

M. furfur, M. minutissimum and Monilia can be differentiated microscopically from other parasites and from each other even if they are intermixed in the same preparation.

Cultures supply the final proof of a combined fungous infection. Their success depends largely on the kind of lesions from which the material is taken. Cultures from the scalp almost always show organisms. When the glabrous skin or the nails are affected the percentage of cultures from cases in which organisms are seen microscopically drops to 50 per cent or less. Cultivation of M. furfur is difficult. M. minutissimum does not grow on any medium.

In cases of combined infection with Monilia and Epidermophyton, microscopic and cultural observations often coincide. They may, however, disagree. In case 5 of my series microscopic examination of the toe webs revealed only filamentous fungi, while cultures produced both E. interdigitale and Monilia. In case 3 of my series a microscopic preparation from the toes showed a mixture of filamentous and yeast-

like fungi, while cultures gave only Monilia. In this case only the yeastlike fungi were found microscopically on the sole, but cultures produced E. interdigitale. In case 4 of my series microscopic examination of the toes revealed filamentous fungi, but cultures gave Monilia.

All such discrepancies are due to the fact that one portion of material is used for microscopic examination and another for cultures. Fungi may be present in one but absent in the other. They may be present "morphologically" but absent "biologically." The microscope shows the organisms even when they are dry and dead. Cultures will grow only from elements having sufficient vitality.

POLYMORPHISM AND PLEOMORPHISM OF PATHOGENIC FUNGI

Isolation of two different fungous colonies from the same patient raises the question whether the organisms really are two different species and not variations of the same species. Such an explanation was suggested by Artom for his case, in which one culture, isolated from an erythematosquamous eruption, was identified as T. glabrum and another, from granulomatous tumors, as T. faviforme. The author admitted that both colonies could have been varieties of the same species which developed different morphologic characteristics owing to the different habitats.

The variability of fungi manifests itself especially in the gross appearance of cultures. Their microscopic structure does not change so easily.

The phenomenon of pleomorphic downy degeneration which occurs in many species of fungi on mediums containing carbohydrates complicates still more the identification of isolated strains. While polymorphism creates unstable variations which eventually return to the primary type, the pleomorphic degeneration is stable and irreversible. The culture changes its appearance beyond recognition and turns into a noncharacteristic white down. Differentiated forms of sporulation disappear and only sterile mycelium remains. A pleomorphically degenerated colony can easily be mistaken for another fungus unless this change is watched for and prevented by transplantation on a medium free from carbohydrates (Sabouraud's "conservation" medium).

THE SAPROPHYTIC EXISTENCE OF PATHOGENIC FUNGI ON THE SKIN

Some observers believe that pathogenic fungi can be accidentally present as saprophytes on a normal skin and in various dermatoses of nonmycotic cause.

Williams [23] examined culturally apparently normal toe webs of 39 persons. In 2 cases cultures of pathogenic fungi were obtained: In

23. Williams, C. M.: The Diagnosis of Some Eruptions on the Hands and Feet, Arch. Dermat. & Syph. **5**:161 (Feb.) 1922.

1, Trichophyton lacticolor was identified; in the other, a fungus resembling E. inguinale.

Cornbleet [24] cultured cutaneous material from the fourth toe web of 100 persons free from any signs of a fungous disease and without a suspicious history. In 2 cases E. inguinale and in 1 case M. audouini were grown.

Downing, Nye and Cousins [25] examined scrapings from the toe webs of 100 persons with apparently normal skin and in 2 cases cultured pathogenic fungi. Contrary to these observations, other investigators reported negative results.

Burgess [26] examined the fourth toe web of 100 persons with normal skin and was unable to demonstrate the presence of ringworm fungi.

Bruhns and Alexander [27] failed to find fungi on the normal feet of 100 persons.

Karrenberg [22] also failed to culture an Epidermophyton from the healthy skin as well as from the skin of patients with eczema, psoriasis and other nonmycotic diseases.

During recent years the pathogenic importance of yeastlike organisms, especially Monilia, in the causation of superficial dermatoses has been recognized, and the same question as to their saprophytic existence on the skin has arisen.

Downing, Nye and Cousins [25] failed to find M. albicans in the apparently normal toe webs of 100 persons.

Benham and Hopkins [28] could not recover Monilia in a series of 100 normal persons. They examined the skin and nails of the fingers, the web between the fourth and the fifth toes and the nails of the great toes.

Lewis and Hopper [29] stated that "Monilia albicans is seldom if ever found on the normal skin."

The following explanations have been suggested for isolation of pathogenic fungi from normal skin: 1. The fungi had just been picked up, had not had time to produce a lesion and were in the incubation

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24. Cornbleet, T.: Cultures from the Skin of Apparently Normal Feet, Arch. Dermat. & Syph. **13**:670 (May) 1926.

25. Downing, J. G.; Nye, R. N., and Cousins, S. M.: Investigations of the Fungous Flora of Apparently Normal Skins, Arch. Dermat. & Syph. **35**:1087 (June) 1937.

26. Burgess, J. F.: Fungous Infections of the Skin, Arch. Dermat. & Syph. **12**:853 (Dec.) 1925.

27. Bruhns, C., and Alexander, A., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 11, pp. 248-249.

28. Benham, R. W., and Hopkins, A. M.: Yeast-Like Fungi Found on the Skin and in the Intestines of Normal Subjects, Arch. Dermat. & Syph. **28**:532 (Oct.) 1933.

29. Lewis and Hopper,[13] p. 128.

period. 2. Since the fungi failed to produce visible signs owing to the resistance of the skin, the patient was a fungus carrier. 3. The patient had previously had attacks of fungous infection with clinical changes of the skin, but the latter had subsided and the fungi had remained in a dormant state, which might be followed by another attack.

THE PATHOGENESIS OF COMBINED FUNGOUS INFECTIONS

A simultaneous infection with two or more different fungi is theoretically possible, but it must be a great rarity under natural conditions. The mode of superinfection is probably the more common one: A person carrying one mycosis acquires the second one later. The occurrence of a fungous superinfection in man stands in contradiction with the results of experimental studies of fungous diseases in animals. The latter acquire immunity even after a superficial mycotic infection. The animal experiments were performed, however, with fungi of great pathogenicity, capable of causing the production of antibodies and the development of immunity. Spontaneous combined fungous infections in man are principally due to the human species of fungi. The results obtained in animals inoculated with virulent fungi cannot be simply transferred to human beings infected with less pathogenic organisms. Even the human species, however, evidently create a considerable degree of immunity because of an obvious rarity of combined infections. This fact is especially noticeable when a wide epidemic of fungous diseases takes place, as, for instance, in Russia in 1922-1926, when many thousands of children were affected and patients with various mycoses were in close contact with each other. Even then, only a few cases of combined infections were observed.

SUMMARY AND CONCLUSIONS

Six cases of combined fungous infections with two different pathogenic organisms present in the same patient are described. In 1 case there was a combination of trichophytosis and favus of the scalp. In the other 5 cases the fungi Epidermophyton and M. albicans were simultaneously present.

Thirty-six similar observations found in the literature are reviewed, and the entire material is discussed from the standpoint of sex, age, location of lesions, proximity of foci due to different parasites, species of fungi, combinations of fungi and succession of mycoses.

The diagnosis of combined fungous infections should be based on cultures. Microscopic examination may suffice in some cases. Clinical pictures alone are unreliable.

Polymorphism and pleomorphism of fungous cultures should be taken into account in the classification of the isolated strains.

Saprophytic existence of pathogenic fungi on the skin, admitted by some observers and denied by others, complicates the problem of the laboratory diagnosis.

The combined fungous infections originate probably by means of a superinfection, although a simultaneous invasion by two or more pathogenic organisms is possible.

The rarity of combined fungous infections suggests the presence of a certain degree of immunity created by the first invader, which protects the patient from a superinfection with another fungus.

HISTOLOGIC STUDIES OF UNINVOLVED SKIN OF PATIENTS WITH PSORIASIS

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A number of years ago I decided to undertake a prolonged study of psoriasis. In previous communications a statistical study and the effects of a low fat diet and of other forms of treatment were reported. In the present paper I shall discuss my investigations on the microscopic structure of the uninvolved skin of psoriatic persons. Although a large amount of work has been done on the typical microscopic changes in psoriasis, the question arose as to whether the skin as a whole took part in the disturbance.

MacKee and Foster [1] stated that 1 in 6 psoriatic patients in their series presented aberrant lesions of psoriasis with typical lesions elsewhere on the skin. Kortanyshev [2] examined microscopically apparently normal skin from the flexor surfaces of the forearms of 25 patients with psoriasis. In 16 he found abnormal changes in apparently normal skin. The changes resembled those found in psoriatic lesions, although they were observed only in certain areas of the excised normal skin. He concluded that in the skin of psoriatic patients pathologic changes are already present before the clinical appearance of a psoriatic lesion and that the corium is affected earlier than the epidermis.

Since the phenomenon of irritation is so well known in psoriasis, it seems reasonable to presume that when psoriasis is in the ascendency the skin must be prepared in some manner to show this abnormal tendency. Therefore, approximately 300 histologic specimens of uninvolved skin of 77 psoriatic patients were studied. These specimens were taken from the favorite sites of psoriasis, from sites where psoriatic lesions rarely occur, from sites of healed psoriatic lesions and from healed centers of active circinate lesions of psoriasis. The general

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From the Ancker Hospital and from the Division of Dermatology and Syphilology, University of Minnesota, Minneapolis, Dr. H. E. Michelson, Director.

1. MacKee, G. M., and Foster, P. D.: Histopathogenesis of Psoriasis and Its Aberrant Lesions, Arch. Dermat. & Syph. **34**:35-56 (July) 1936.

2. Kortanyshev, A. I.: Histopathologic Character of Apparently Healthy Skin in Psoriatic Patients, Vestnik ven. i dermat., 1939, no. 1, p. 30; abstracted, Arch. Dermat. & Syph. **40**:813 (Nov.) 1939.

histologic structure of the skin, as well as the connective tissue, elastic tissue and fat, was studied. The histologic sections of skin from psoriatic patients were compared with histologic sections of normal skin taken from the same sites of patients who did not have psoriasis. The patients received no external or internal medication for at least one month before biopsies were made. All types of psoriasis were studied except psoriasis arthropathica and pustular psoriasis. The patients ranged in age from 6 to 76 years, and there were about equal numbers of the two sexes. The duration of the eruption varied from two months to thirty years. All the sections were stained with hematoxylin and eosin unless otherwise stated.

TYPICAL PSORIATIC LESION

Nobl,[3] Gans,[4] McCarthy,[5] Montgomery[6] and MacKee and Foster[1] portrayed a fairly uniform picture of the typical lesion of psoriasis. The epidermis is thickened, and the increased depth is seen mostly in the rete pegs. There is a loose, lamellar hyperkeratotic scale alternating with islands of parakeratosis. The scale varies in thickness, and the parakeratosis is always present. The granular layer is not lost but may be irregular, and at times it seems to alternate with the parakeratosis. There is proliferation of the prickle cell layer, and the rete pegs are longer and usually broader than normal. Acanthosis is most evident in the rete pegs. The prickle cells are often pale and swollen, and the nuclei become flattened or crescentic and migrate to the edge of the cell. The basal cell layer is often frayed and irregular, and the borderline of the epidermis and cutis may be blurred owing to edema. Polymorphonuclear leukocytes wandering singly, in strands or in groups throughout the epidermis are a constant observation in psoriasis. When the leukocytes are seen in groups they are called Monro-Sabouraud abscesses. These abscesses may be seen anywhere in the epidermis but are usually found between the lamellas of the horny layer or between the horny and the prickle cell layer. The papillary bodies are lengthened and are capped by only three or four layers of prickle cells in some cases. The blood vessels are greatly dilated and engorged, and the lymph spaces are dilated. There is a lymphocytic and polymorphonuclear leukocytic infiltrate, which is diffuse but mostly perivascular. There is a varying

3. Nobl, G.: Psoriasis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, p. 180.

4. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 280.

5. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 194.

6. Montgomery, H.: Exfoliative Dermatosis and Malignant Erythroderma, Arch. Dermat. & Syph. **27**:253-276 (Feb.) 1933.

degree of edema. The changes in the cutis are almost entirely in the upper half. Edema is prominent, and the connective tissue bundles are separated and rich in fibroblasts. The lymph spaces are dilated, and the blood vessels are dilated and engorged. There is a lymphocytic, mast cell and polymorphonuclear leukocytic infiltrate, which is diffuse but mostly perivascular. The adnexa and the elastic tissue are not affected. The tissue below the middle portion of the cutis is usually normal.

UNINVOLVED SKIN FROM FAVORITE SITES OF PSORIASIS

Sixty-four specimens of uninvolved skin were studied from the sites of election in 32 psoriatic patients. The specimens were taken from the skin of the elbow, knee, sacrum, scapula, abdomen and extensor surface of the forearm and thigh. They were never taken from near a psoriatic lesion.

There was hyperkeratosis which seemed to be within normal limits, and parakeratosis was not seen. The epidermis was not thickened, and the granular layer was normal. Some of the nuclei of the prickle cells were crescentic or flattened and had migrated to the edge of the cell in every case. This observation was striking in over half of the cases and did not occur in any special type of psoriasis; however, these nuclear changes were noted in the normal skin of nonpsoriatic persons, so no significance was attached to them. The rete pegs were elongated in the 5 cases of acute guttate psoriasis but were normal in the other types. The basal cell layer was normal, and there was no evidence of edema in the epidermis. The most striking abnormality in the histologic picture of the uninvolved skin was the increased infiltrate, which was of the same type as seen in a typical psoriatic lesion. The infiltrate was most pronounced and was always present in the uninvolved skin of patients with acute guttate and generalized papular psoriasis. In cases of psoriasis in which the lesions were limited to a few plaques of long standing there was little or no increase in infiltrate. Single leukocytes wandered freely throughout the epidermis, but no Munro-Sabouraud abscesses were seen. The infiltrate occurred diffusely and in a perivascular manner in the papillary bodies and in the upper half of the cutis. When the infiltrate was great, the capillaries were dilated and engorged, and the papillary bodies were elongated and pushed toward the surface. In these instances there were slight edema of the upper half of the cutis and an increase in fibroblasts. It was evident that histologic changes simulating but less pronounced than those seen in a typical psoriatic lesion occurred in the uninvolved skin taken from sites of election in patients with acute guttate and generalized papular psoriasis. These changes were not found in uninvolved skin from the chronic stationary plaques.

UNINVOLVED SKIN FROM SITES WHERE PSORIASIS RARELY OCCURS

Thirty-four specimens of uninvolved skin were studied from the popliteal and cubital spaces of 17 psoriatic patients.

Here again the changes previously described in the nuclei of the prickle cell layer were noted. The 8 specimens from 4 patients with acute guttate and generalized papular psoriasis showed the same changes as seen in uninvolved skin from sites of election in similar cases. The infiltrate was similar in type and degree and was accompanied by capillary dilatation, elongation of rete pegs, lengthening of papillary bodies, with pushing toward the surface, and slight edema. No change was seen in sections from patients with other types of psoriasis. The uninvolved skin of patients with acute guttate and generalized papular psoriasis showed inflammatory changes, as previously described, at sites where psoriatic lesions rarely occur as well as at sites of election.

UNINVOLVED SKIN FROM SITES OF HEALED LESIONS

Thirty specimens of uninvolved skin were studied from healed lesions of 15 psoriatic patients. In order to determine the proper sites for removal of specimens for biopsy, it was necessary to rely on the patient's accuracy and honesty in 9 cases, but this was substantiated by definite hyperpigmentation in the other 6 cases. All of the lesions had been healed for at least one month, and in 1 case hyperpigmentation had remained at the sites of former lesions for over a year. The acute guttate and generalized papular types were not considered here because of the obvious improbability of remembering the location of such small lesions.

The sections taken from the sites which showed normal pigment were normal in other respects. The sections taken from the hyperpigmented sites showed a definite leukocytic infiltrate, dilatation of the capillaries, lengthening of the rete pegs and papillary bodies and slight edema of the upper part of the corium, such as was seen in the uninvolved skin of patients with acute guttate and generalized papular psoriasis both at the sites of election and at the sites where psoriasis rarely occurs. It is possible that hyperpigmentation as well as other phenomena of irritation preserve "cellular memory" in psoriasis. Kissmeyer's [7] case of the girl whose brother scratched his initials on the back of her hand with a pin two years before psoriatic papules developed outlining the initials is one of the classic instances of "cellular memory."

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7. Kissmeyer, A.: Rôle du traumatisme antérieur et "mémoire cellulaire" dans le psoriasis, Ann. de dermat. et syph. **5**:1085-1088 (Dec.) 1934.

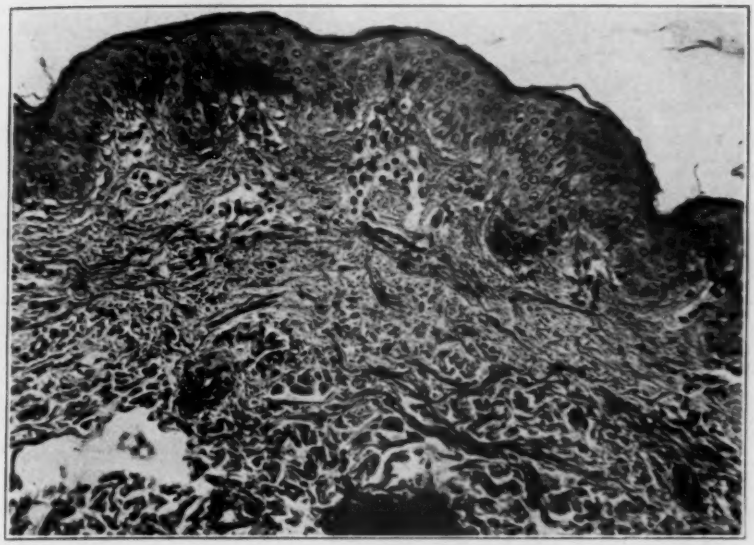


Fig. 1.—Uninvolved skin from a site of election just proximal to the elbow in a case of acute psoriasis, showing wandering leukocytes in the epidermis, infiltration in the upper part of the corium and dilated blood vessels.

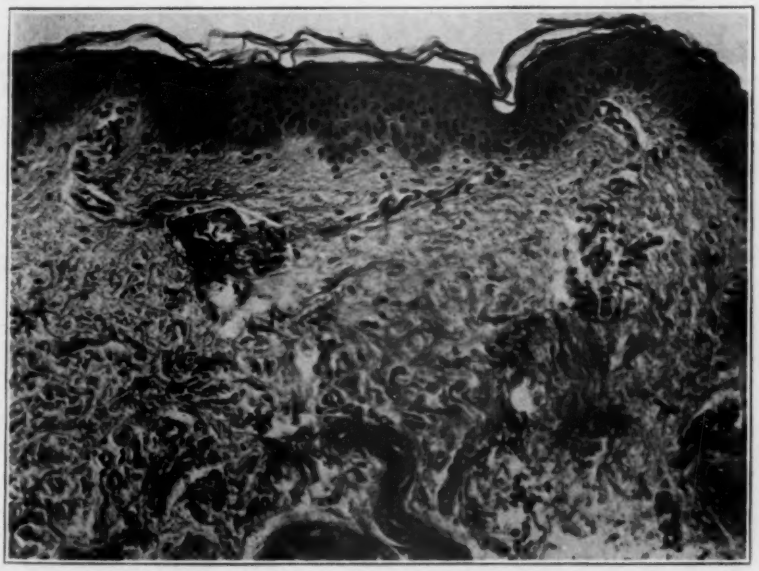


Fig. 2.—Uninvolved skin from a cubital space, showing perivascular infiltration in the upper part of the corium.

SKIN FROM HEALED CENTERS OF ACTIVE CIRCINATE LESIONS

Twenty-six specimens were studied from healed centers of active circinate lesions in 13 psoriatic patients. The lesions were all healing or stationary, and the psoriasis as a whole was in a stationary or descending phase.

The 22 sections from normally pigmented centers showed no abnormality. Three sections from healed pigmented centers showed a moderate leukocytic infiltrate, dilatation of the capillaries and elongation of the rete pegs and papillary bodies. However, these changes were evident to a less degree than at the sites of election and the sites where psoriasis rarely occurs, as well as the sites of pigmented healed plaques. Temporary local immunity in the healed centers, which was partially overcome by the possible irritation of the pigment or the noxae which caused the production of pigment, could explain these observations. One section from a pigmented center which had been healed for three months showed a typical histologic picture of psoriasis. Evidently psoriasis can be present histologically for a long time after it has healed clinically. This may account for the not infrequent necessity of treating psoriasis long after the clinical lesion has disappeared.

SPECIAL STUDIES OF THE UNINVOLVED SKIN

The elastic tissue, connective tissue and fat were studied in the uninvolved skin from the sites of election in 32 psoriatic patients. The elastic tissue was stained with the Weigert stain, the connective tissue with the Van Gieson stain and the fat with sudan III. The elastic tissue was normal, and the connective tissue was normal except that it seemed rich in fibroblasts in the 5 cases of acute guttate and generalized papular psoriasis.

It was realized early in the study that ordinary methods of staining fat did not give any information which in any manner clearly differentiated psoriatic from normal skin. Because of previous work which had emphasized abnormalities of the fat in psoriatic lesions, the sections were all stained with sudan III, and the observations were as follows: There was a definite increase in the amount of fat seen in all sections from the sites of election, such as the skin of the elbow, knee, sacrum, forearm, shin, scapula and abdomen, when compared with sections from the same sites in nonpsoriatic persons. There seemed to be much more fat in the scale of the uninvolved skin of the psoriatic patient, as well as in the skin from the other points of concentration of fat, namely, in and around the pilosebaceous apparatus and sweat glands. The fat did not seem to be greatly increased around the blood vessels. Fat was plentiful throughout the corium and was practically

Fig. 3.—Uninvolved skin from the hyperpigmented site of a lesion which had been clinically healed for six months. Note the upward flow of leukocytic infiltration, which is mostly perivascular, the lengthened rete pegs, the elongated papillary bodies and the dilated and engorged blood vessels.

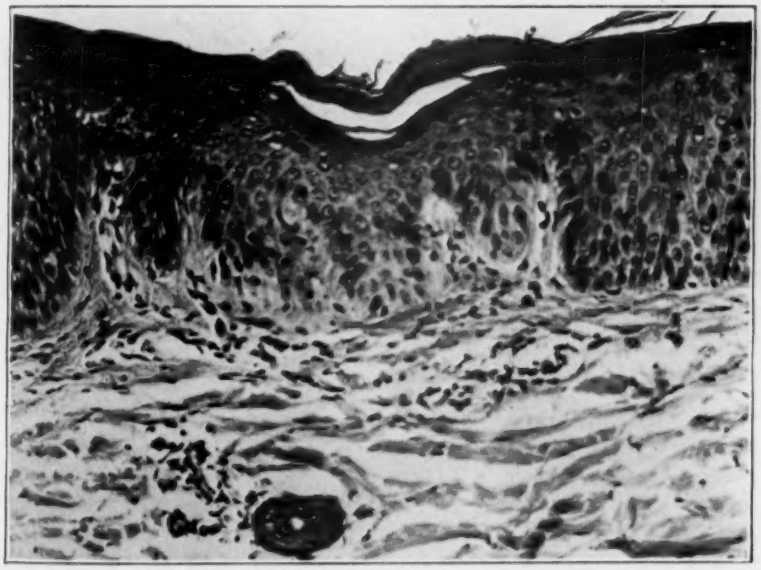


Fig. 4.—Hyperpigmented skin from the clinically healed center of an active circinate lesion of psoriasis. The center had been clinically healed for three months. Note the parakeratotic scale, the wandering leukocytes in the epidermis, the elongated rete pegs, the lengthened papillary bodies and the upward sweep of the infiltrate in the upper part of the corium.

always extracellular. The same observations were made when 15 specimens were studied from the popliteal and cubital spaces, hyperpigmented sites of healed lesions on the extremities and buttocks and healed centers of active circinate lesions of the extremities. However, 5 specimens from the skin distal and posterior to the ear, skin from the upper third of the sternum and skin from the nape of the neck of psoriatic patients were compared with an equal number of specimens from the same places in nonpsoriatic persons, and the amount of fat appeared to be the same in all cases. From these studies it seems that there is an increase in the amount of fat in the skin of psoriatic patients in places where the sebaceous glands are few. When specimens are taken from the areas with abundant sebaceous glands the fat is so pronounced in both psoriatic and nonpsoriatic persons that comparison is futile. Grütz [8] found lipophages abundant in the thick, scaly plaques of patients with the acute inflamed types of psoriasis. He saw the lipophages wandering through the epidermis and corium carrying fat; however, he stated that most of the fat was extracellular. No such cells were encountered in this study, possibly because different stains may have been used.

COMMENT AND SUMMARY

Approximately 300 histologic specimens from the uninvolved skin of 77 psoriatic patients were studied.

The presence of leukocytic infiltrate, capillary dilatation, lengthening of the rete pegs and papillary bodies in the uninvolved skin at the sites of election, as well as at sites where psoriasis rarely occurs, indicated that the skin as a whole took part in the disturbance. These observations were constant in patients with acute guttate and with generalized papular psoriasis.

Flattened and crescentic nuclei migrating to the edge of the prickle cells were seen both in the uninvolved skin of psoriatic patients and in the skin from normal persons; so the observation was considered insignificant.

Histologic changes simulating, but less pronounced than, those seen in a typical psoriatic lesion occurred in the uninvolved skin of persons with acute guttate and generalized papular types taken from sites of election and from rare sites for psoriatic lesions as well as from hyperpigmented patches at the sites of healed psoriatic lesions and from hyperpigmented healed centers of active circinate psoriatic lesions. The presence of pigment or of the noxae which stimulated formation of pig-

8. Grütz, O.: Neue histologische Beiträge zum Psoriasis-problem, Arch. f. Dermat. u. Syph. **177**:246-252, 1938.

ment must have been an important factor in the changes noted in the two last-mentioned locations. These inflammatory changes seem to indicate that the noxa which causes psoriasis is blood borne and that the corium is attacked before the epidermis.

The presence of a typical histologic picture of psoriasis in the skin of a pigmented center which had been healed for over three months indicates that psoriasis can be present histologically long after it has healed clinically. This may account for the not infrequent necessity of treating psoriasis long after the clinical lesion has disappeared.

The elastic tissue and the connective tissue were normal except for a questionable increase in fibroblasts in the connective tissue of 5 patients with acute guttate and generalized papular psoriasis.

The fat was increased in the uninvolved skin in psoriasis with the possible exception of the areas where sebaceous glands were abundant. Where the sebaceous glands were plentiful the fat was so thick both in psoriatic and in normal persons that a comparison was futile. The fat was most abundant in the scale, in the pilosebaceous apparatus and in and around the sweat glands. There was not a great increase in fat about the blood vessels, and lipophages were not seen. The fat was almost always extracellular. Further studies with special staining methods should be carried out before a decision is made concerning the role of fat in the histologic structure of persons with psoriasis.

ABSTRACT OF DISCUSSION

Dr. Martin F. Engman Jr., St. Louis: I think it is important to comment on the viewpoint that Dr. Madden has taken with regard to psoriasis. He has examined not only the lesion but also the unaffected, uninvolved skin of persons who have this disease. This is not an entirely new idea.

Many years ago Gilchrist and Philipson studied the unaffected skin of persons with urticaria. In about 1905 Engman Sr. reported studies of the unaffected skin of persons with epidermolysis bullosa. My associates and I in the last three years have studied the unaffected skin of persons with neurodermatitis and with some other disease and also normal skin of normal persons. We consider that the unaffected skin is a fertile field that has been neglected, to a great extent, in so many researches on disease of the skin. We are also interested in the study of psoriasis, both the affected and unaffected skin, by the methods of micro-incineration and spectrographic analysis, as well as histologic examination, but we have nothing to report at this time.

Dr. Samuel F. Sweitzer, Minneapolis: I have been interested in Dr. Madden's study of psoriasis, which he has been doing for many years. I was particularly interested in the phase of the fat content of the cells, because for many years in my own practice in the clinic I have limited the fat intake of patients with psoriasis. I did not know whether there was any basis for this or not, and I had hoped that Dr. Madden would show some relation, but, unfortunately, the fat phase of this study did not come out as expected.

I think it is interesting to note from Dr. Madden's studies that psoriasis is apparently a disease that affects the entire skin. That would lead one to the conclusion that it is probably not an infection; it might be assumed that the disease was caused by a disturbance of the metabolism or some other internal process.

Dr. William H. Goeckerman, Los Angeles: I think Dr. Madden's work should receive full recognition; so far as I know, such work has not been done anywhere before. Of all the etiologic theories for psoriasis suggested throughout the years, as Dr. Sweitzer said, none of them has as yet been proved. It seems as though one will have to come back to the old conception of diathesis. That the study is along the right direction, I think, is further suggested by the familiar fact that usually the psoriatic patient is of the asthenic, upstanding, thick-necked and thick-limbed type. One seldom sees a decrepit type of person showing psoriatic lesions, at least not in the early years of life. Furthermore, I think these studies may be of clinical value in cases in which psoriasis has become generalized and exfoliative and cannot be clinically differentiated from eczematoid dermatitis; it is now possible by histologic examination of skin from almost anywhere on the body to make a diagnosis of antecedent psoriasis, knowing nothing about the history.

I think Dr. Madden should be encouraged to continue his studies.

Dr. Samuel M. Peck, New York: I wish to congratulate Dr. Madden on his excellent presentation. I believe that it throws a light on this baffling condition. The two main theories for the cause of psoriasis are the parasitic and the metabolic. One of the mainstays of the parasitic theory has been the Köbner phenomenon: When the unaffected skin of a patient with a spreading psoriasis is scratched, the disease localizes in the area of trauma. This was only supposed to occur in parasitic conditions, especially when there was a circulating noxa. This is now known to be not absolutely true, and I think that Dr. Madden's work supports this doubt.

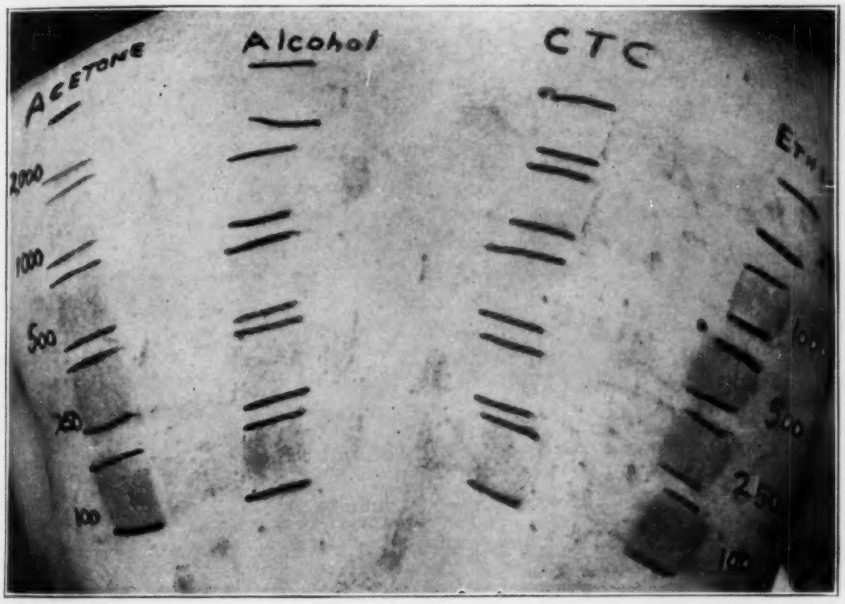
If the entire skin is always involved but the condition is not clinically manifest, then it is important that the body as a whole should be treated and not just single lesions.

Dr. Lee McCarthy, Washington, D. C.: In order to give the other side of the question of causation, I should like to call attention to the work of Lindenberg (Lindenberg, A.: Un nouveau point de vue dans l'étude étiologique des dermatoses, *Ann. de dermat. et syph.* **9**:929 and 1025, 1938). He was invariably able to reproduce psoriasis in guinea pigs and rabbits by injecting tissue solutions in the testicle of these animals. Psoriasis developed in his experimental animals in from six weeks to six months. This disease was confirmed by histologic examination. I do not believe his work has been confirmed to date.

SOLUBILITY OF THE DERMATITIS-PRODUCING FRACTION OF POISON IVY

J. B. HOWELL, M.D.
DALLAS, TEXAS

The allergenic potencies of oleoresins extracted from portions of a single ivy plant vary according to the fat solvents employed for extraction of the oil. The dermatitis-producing fraction of the oleoresin is



Reactions to patch tests with ivy oleoresins extracted with various solvents.

highly soluble in ether and only slightly less soluble in acetone. Dehydrated alcohol and carbon tetrachloride produce oleoresins approximately one fifth to one tenth as potent, according to biologic tests, as those extracted with ether or acetone. The solvent employed for extraction of ivy oleoresin is of paramount importance, since dilutions of ivy oleoresins employed for quantitative patch tests or for oral therapy may vary 1,000 per cent in potency, depending on the fat solvent employed for extraction of the oil.

METHOD

Leaves from a single plant of Rhus toxicodendron radicans were collected and dried at room temperature for two weeks. After thorough drying, 120 Gm. of leaves was triturated and divided into four parts of 30 Gm. each. Each mass

was placed in a pint jar and covered with equal amounts (by volume) respectively of ether, acetone, carbon tetrachloride and dehydrated alcohol. After standing for forty-eight hours the solvents were removed, passed through ordinary filter paper and placed in open vessels; evaporation was then allowed to take place.

The solvent-free residues were then diluted with corn oil, by volume, to make dilutions of 1:100, 1:250, 1:500, 1:1,000 and 1:2,000 for quantitative patch tests. Simultaneous patch tests with the quantitative dilutions of the oleoresins prepared with the four solvents were made on the back of a subject in lines parallel with the spinal column. Exactly 2 drops of each dilution was placed on the test site, and the area was covered with a small square of gauze held in place with adhesive tape. Coverings were removed after exactly twenty-four hours, and final reading was made on the fourth day.

Reactions to Quantitative Tests with Ivy Oleoresins Extracted with Various Solvents

	Acetone					Alcohol					Carbon Tetrachloride					Ether				
Subject	1:100	1:250	1:500	1:1,000	1:2,000	1:100	1:250	1:500	1:1,000	1:2,000	1:100	1:250	1:500	1:1,000	1:2,000	1:100	1:250	1:500	1:1,000	1:2,000
D. J.	4+	2+	±	—	—	2+	—	—	—	—	2+	—	—	—	—	4+	2+	+	—	—
R. S.	3+	2+	2+	±	—	3+	+	+	—	—	+	—	—	—	—	3+	2+	2+	+	—
R. H.	4+	4+	2+	±	—	2+	±	—	—	—	2+	+	—	—	—	4+	4+	3+	+	—
F. G.	4+	4+	4+	+	—	2+	+	—	—	—	+	—	—	—	—	4+	4+	4+	4+	±
S. E.	3+	2+	±	—	—	+	—	—	—	—	+	—	—	—	—	3+	3+	2+	+	—
A. S.	3+	2+	+	—	—	±	—	—	—	—	—	—	—	—	—	3+	2+	+	±	—
P. B.	+	±	—	—	—	±	—	—	—	—	±	—	—	—	—	+	±	—	—	—
J. I. V.	2+	+	±	—	—	+	—	—	—	—	±	—	—	—	—	2+	+	+	—	—
H. S.	+	±	—	—	—	±	—	—	—	—	±	—	—	—	—	2+	+	±	—	—
J. C.	+	+	—	—	—	+	—	—	—	—	—	—	—	—	—	2+	+	±	—	—

RESULTS

The accompanying illustration shows how widely these solvents vary in extracting the dermatitis-producing fraction of poison ivy.

The results of patch tests in 10 persons with varied sensitivity are given in the table.

CONCLUSION

Absolute alcohol and carbon tetrachloride produce oleoresins approximately one fifth to one tenth as potent as those extracted with ether or acetone. The dermatitis-producing fraction of the oleoresin is highly soluble in ether and only slightly less soluble in acetone.

SYPHILIS OF THE LARYNX

REPORT OF AN ATYPICAL CASE

LEON FELDERMAN, M.D.
PHILADELPHIA

The case reported is of interest because of the difficulties encountered in differentiating syphilis from cancer when the condition involves the larynx.

REPORT OF CASE

J. F. C., a man aged 57, an engineer, consulted me in May 1937. He complained of intermittent loss of voice for the previous twelve years, a condition which had become progressively worse during the last five years.

He suffered from Buerger's disease in 1926, from which he seemed to have recovered. He was operated on for bilateral polypoid ethmoiditis in 1928. In 1932 he was exposed for about fifteen minutes to inhalation of chlorine gas, resulting in hoarseness which persisted almost without remission. He was the "chain type" cigaret smoker and drank in moderation. He stated that he had not suffered from any venereal disease.

Examination of the nose revealed an intense red schneiderian membrane, with chronic involvement of the posterior group of sinuses. The sinuses were treated, with good results, with silver picrate, 1 per cent in dextrose solution. The indirect mirror inspection of the larynx showed an epiglottis somewhat fixed in movements, making it difficult to examine the larynx, but the application of a local anesthetic made it possible to obtain a better view. The arytenoids appeared inflamed and enlarged. The vocal cords were red, thick and limited in motion. No growth of any kind could be distinguished. In spite of negative reactions to serologic tests, including a test of the spinal fluid, my provisional diagnosis was syphilis of the larynx. This diagnosis was based on intermittent hoarseness for twelve years, fixation of the epiglottis, limited motion of one of the cords, a uniform deep red color of the vocal cords and total freedom from pain. When intramuscular injections of a bismuth compound were administered, an interesting change took place: The epiglottis and the arytenoids moved with comparative ease, and the voice became less hoarse.

The patient then consulted another laryngologist, who made a diagnosis of "squamous cell carcinoma, intermediate type III," based on the histologic study of tissue. His observations introduced a different aspect of the matter.

The results of an examination by a radiologist on March 1, 1938 were summed up as follows:

"There is no roentgen ray evidence of pulmonary or secondary neoplasm of either lung. There is no evidence of acute or unhealed pulmonary tuberculosis. The heart is normal in size, outline and position. The supracardiac shadow is slightly widened, but this is probably due to elongation of the aorta. The diaphragmatic domes are normal in outline and position. The thyroid cartilages show considerable calcification. There is a moderately dense shadow in the region

of the ventricle and vocal cords. The epiglottis, the vallecula and the vestibule are normal. In view of the increased density of the region of the ventricle and vocal cords, the possibility of an intralaryngeal lesion must be considered."

On March 21, 1938 the patient was referred to a medical consultant, who reported as follows:

"The cardiac hypertrophy and hypertension, the hepatic enlargement, the adenopathy, including large epitrochlear glands (though no cervical adenopathy), and the aortitis, combined with the preservation of good health for several years, the gain in weight and the improvement under bismuth medication, justify the diagnosis of syphilis of the larynx rather than of a malignant condition."

About this time the result of a Gruskin test for malignancy was negative.

However, the patient, dissatisfied with the conflicting views, consulted still another laryngologist. His diagnosis, after examination and review of the slides made of the previously taken biopsy specimen, was that of cancer. It therefore seemed best to adopt the combined roentgen ray and radium therapy advised by the laryngologist then in charge. On April 2, 1938 a roentgenogram showed a tumor involving the left arytenoid, the left vocal cords measuring approximately 1.5 cm. A roentgenogram taken on September 26 revealed edema of all tissues within the laryngeal cavity. He was treated with roentgen rays and radium from April 15 to November 2.

A summary of a letter from the hospital is as follows:

"Mirror examination of the larynx on the patient's first visit, in April 1938, showed the left side to be involved in an ulcerative process, with fixation of the cord, the right side being grossly normal. He was again seen in June, after a course of irradiation, at which time the right cord still appeared normal but the left showed some deformity due to destruction as a result of the neoplastic ulceration, but no tumor was demonstrated on gross inspection. There was some edema of the left arytenoid and aryepiglottic fold. The patient in September complained of pain and cough. At that time there was edema of the arytenoids and of the aryepiglottic fold on the left side. In October the appearance of the larynx was essentially the same. But on November 3 the patient was admitted to the hospital because of difficulty in swallowing and some dyspnea. At that time a nasal feeding tube was passed, and three days later a tracheotomy became necessary because of laryngeal obstruction. For about ten days following tracheotomy the patient's breathing was improved. However, on November 16 he had a sudden rise in temperature and began to cough up a large amount of foul material. He then became progressively worse and died on November 26."

The postmortem observations were as follows:

	Anatomic	Microscopic
Heart	Myocardial degeneration; atherosclerosis of the coronary arteries; healed myocardial infarct	Fibrosis of the myocardium; atheroma of aorta; necrosis
Aorta	Atherosclerosis of the aorta; syphilitic aortitis	
Lungs	Gangrenous pneumonia	Gangrenous pneumonia
Larynx, trachea	Gangrenous laryngotracheitis	Necrosis of laryngeal cartilage; chronic laryngitic tracheitis
Spleen	Congestion	Congestion; arteriosclerosis
Kidneys	Congestion	Renal arteriosclerosis
Liver	.....	Parenchymatous degeneration
Mediastinum	.....	Chronic lymphadenitis

The postmortem report pointed to syphilis, but no sign of cancer was detected anywhere.

COMMENT

The larynx is highly susceptible to syphilitic infection, which is manifested by persistent chronic hoarseness of a dry character. The condition appears to be more frequent in men than in women. Although primary infection of the larynx is rare, secondary infection is occasionally seen, and perichondritis of the larynx is the only manifestation of the tertiary type. The occurrence of syphilitic infection of the larynx is common in the third or fourth decade of life. Among the predisposing causes is the use of alcohol and tobacco. The tertiary form of syphilis may appear in the second or third year, as the lesion may be delayed for many years, but when it does appear, it may take on any of these forms: (1) gumma and gummatous infiltration, (2) ulceration, (3) perichondritis and necrosis, (4) postsyphilitic induration or (5) syphilitic scars and adhesions. Persistent hoarseness may be the only symptom.

Syphilis of the larynx has been mentioned by some authorities as appearing in two forms, (1) gumma and (2) diffuse syphilis. The syphilitic gumma is round or oval and is difficult to distinguish from tuberculosis. The pattern of giant cells, lymphocytes and plasma cells can be distinguished. Also the granulomatous architecture has vascularization in contrast to the tuberculous lesion, which is avascular. The diffuse type of syphilis is more polymorphous. It is hypertrophic or hypoplastic. One finds on microscopic examination leukocytes and plasma cells. The preponderance of the latter cells is a diagnostic feature of syphilis.

The distribution of the syphiloma is diffuse and variable. Sometimes the progression of the lesion from the muscle to the cartilages of the larynx is orderly. The granuloma of syphilis characteristically builds mainly around the blood vessels until all are involved.

Not infrequently the disease is taken for epithelioma. All granulomas of syphilitic origin grow rapidly. They are different from those of tuberculosis, especially in the diffuse type of syphilis, in which the tissues undergo necrosis, leaving ulcerations which are irregular and funnel shaped. Some of the symptoms are respiratory. When the asphyxiation is intense, especially on inspiration, the vocal cords are fixed, owing to the infiltration. They often appear extremely red, a highly significant sign in syphilitic infections.

SUMMARY AND CONCLUSIONS

A case of typical syphilis of the larynx is reported. In spite of negative reactions to serologic tests, the condition was first diagnosed as laryngeal syphilis. The diagnosis was based on a history of chronic hoarseness, a fixed epiglottis limited in motion, failure to lose weight, the response to treatment, the medical report and a negative reaction to

a Gruskin test. Two well known laryngologists made the erroneous diagnosis of laryngeal cancer, on which the treatment was based. The patient was given intensive radium therapy but at no time reported improvement. On the contrary, he complained of excruciating pain referable to the region of the middle ear.

The lesson from this case is that no single finding should be relied on for a diagnosis; on the contrary, the diagnostician should study carefully all the symptoms of his patient. When doubt exists, as it did in this case, intensive antisyphilitic treatment should first be administered, and if the symptoms do not ameliorate within a reasonable time, then a more radical procedure should be considered.

1737 Chestnut Street.

URTICARIA DUE TO TRYPARSAMIDE

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NASHVILLE, TENN.

Untoward effects resulting from tryparsamide are relatively infrequent. Cutaneous reactions to the drug have been occasionally reported. They have appeared after few and after a great many injections. Ebaugh and Dickson [1] in 1924 were the first to mention mild dermatitis due to tryparsamide. This comment was made casually in a paper on the use of the drug in the treatment of dementia paralytica. There have been four reports of mild exfoliative dermatitis [2] and two of unqualified exfoliative dermatitis.[3] A fixed dermatitis due to tryparsamide has also been described in four reports.[4] One case in which herpes zoster appeared after several injections of tryparsamide has been reported.[5] Ellis [6] reported a case in which a papular eruption developed which became covered with serosanguineous crusts after the use of tryparsamide. Twelve cases in the literature have been labeled merely cases of "dermatitis," the type of lesion not having been described.[7]

From the Department of Medicine, Vanderbilt University School of Medicine.

1. Ebaugh, F. G., and Dickson, R. W.: The Use of Tryparsamide in the Treatment of General Paralysis, J. A. M. A. **83**:803 (Sept. 13) 1924.

2. (*a*) O'Leary, P. A., and Becker, S. W.: Further Observations on the Treatment of Neurosyphilis with Tryparsamide, M. J. & Rec. **123**:305 (March 3) 1926. (*b*) Phelps, J. R.: Reactions Incidental to the Administration of 191,778 Doses of Neoarsphenamine and Other Arsenical Compounds in the United States Navy, U. S. Nav. M. Bull. **27**:205 (Jan.) 1929. (*c*) Robinson, S. S.: Dermatitis Due to Tryparsamide, Arch. Dermat. & Syph. **34**:251 (Aug.) 1936. (*d*) Nair, V. G.: Exfoliative Dermatitis After Tryparsamide, Indian J. Ven. Dis. **3**:13 (March) 1937.

3. (*a*) Bragman, L. J.: Tryparsamide Dermatitis, Am. J. Syph. & Neurol. **18**: 308 (July) 1934. (*b*) Golz, H. H.: Sensitivity to Arsenical Drugs, Am. J. Syph., Gonor. & Ven. Dis. **23**:344 (May) 1939.

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5. Rosenberg, W. A.: Bilateral Asymmetrical Herpes Zoster Following Tryparsamide Therapy, Illinois M. J. **74**:164 (Aug.) 1938.

6. Ellis, F. A.: Tryparsamide Dermatitis, Am. J. Syph., Gonor. & Ven. Dis. **22**:336 (May) 1938.

(Footnotes continued on next page)

The first mention made in the literature of an urticarial reaction following the use of tryparsamide appeared in a paper by Kopp and Solomon [4d] in 1940. Among 829 patients who were given a total of forty-three thousand, three hundred and eight injections of tryparsamide were 5 who had had urticaria. The first patient had generalized urticaria after nine injections of the drug. Later, after twenty-five injections of neoarsphenamine, exfoliative dermatitis developed. The second patient had urticaria after the twentieth injection of tryparsamide and a year later was given the drug without any recurrence. In the third patient urticaria was brought on by the forty-eighth injection of tryparsamide. This reappeared after twenty-five injections of neoarsphenamine. Urticaria developed in the fourth patient following the thirty-fourth injection of the drug. The fifth patient merely had "swelling of the face" after four hundred and twenty-one injections.

The following report is that of a case in which recurrent generalized urticaria was apparently due to tryparsamide.

REPORT OF A CASE

Mrs. M. P., a 41 year old white woman, was admitted to the medical clinic of Vanderbilt University Hospital in December 1933. For two years she had noted motor disturbances of the right lower extremity, with progression during the previous year before admission. Conscious effort was necessary in the use of the extremity. A limp and some staggering were noted, but no subjective sensory disturbances were referred to the limb. One year before admission the patient had experienced a probable transient hemiparesis of the right arm and face. This was accompanied by a temporary difficulty in speaking. There was no past history suggestive of syphilitic infection.

The physical examination revealed the following abnormalities: There was hyperactivity of the right knee jerk. Babinski, Gordon and Oppenheim signs could be elicited on the right side. There was some spasticity of the muscles of the right lower extremity. The Wassermann and Kahn reactions of the blood were consistently positive. Examination of the spinal fluid showed a positive reaction for globulin, 6 cells per cubic millimeter, a positive Wassermann reaction in 1.0, 0.5, and 0.2 cc. dilutions and a 5555543210 colloidal mastic curve.

The clinical diagnosis was spastic monoplegia due to cerebral vascular syphilis.

Antisyphilitic treatment was begun in January 1934, with improvement in the gait in about seven weeks. In the following sixteen months the patient received forty-five injections of bismuth subsalicylate, twenty-eight injections of old arsphenamine (0.3 Gm. per dose) and six injections of neoarsphenamine (0.6 Gm. per dose) on an intermittent plan of treatment.

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7. (*a*) Keith, T. S., and LeMarquand, H. S.: Some Notes on Tryparsamide Therapy in a Venereal Disease Clinic, Brit. J. Ven. Dis. **5**:38 (Jan.) 1929. (*b*) Lichtenstein, J. V.: Tryparsamide Therapy: A Follow-Up Report on Seventy-Six Patients with Neurosyphilis Treated with Tryparsamide, Arch. Dermat. & Syph. **24**:182 (Aug.) 1931. (*c*) Cole, H. N., and others: Toxic Effects Following Use of the Arsphenamines, J. A. M. A. **97**:897 (Sept. 26) 1931. (*d*) Robinson.[4a] Kopp and Solomon.[4d]

In July 1935 the patient was given tryparsamide on four occasions, the first two doses consisting of 1 Gm. and the last two of 2.5 Gm. Administration of this drug was stopped after a complaint of blurred vision. The spinal fluid picture having been changed relatively little, routine continuous treatment with trivalent arsenicals and a bismuth compound was carried out in the succeeding fifteen months. Fever therapy was refused.

In December 1936 tryparsmide was again tried, three doses of 3 Gm. each being given during that month. Nothing unusual was noted after the first of these injections. After the third injection the patient reported a cutaneous reaction appearing forty-eight hours after the injection. First there was intense itching of the hands, which then became swollen. The lips became edematous, and the thighs became swollen, itched and were covered with pink splotches. The condition became so intense that a physician was called, who relieved it by the use of epinephrine. At the time the patient reported this reaction she stated she had had the same type of reaction, though less intense, following the second dose of tryparsamide in this course and had failed to report it to me. Furthermore, she recalled having had similar symptoms and signs at the time tryparsamide was used in July 1935, which she had also failed to report.

A patch test with tryparsamide elicited a negative reaction. In February 1937 a 1 Gm. dose of the drug was given without trouble. Then a 3 Gm. dose was given, and again forty-eight hours later an itching eruption appeared, described as urticarial as on the previous occasion.

In May 1937 tryparsamide was again given in a 1.5 Gm. dose, without reaction. Twenty-four hours after a 3 Gm. dose the patient had the usual reaction. There were itching and swelling of the lips. A sense of constriction was present in the chest for the first time. Itching was generalized, and urticarial wheals appeared on the neck, abdomen, arms and thighs. A blotchy erythema accompanied the urticaria.

No more treatment was given, since the patient refused fever therapy. She was seen at intervals between the time of the last reaction and her last visit to the clinic in September 1940 for examination of the spinal fluid. There was no recurrence of urticaria at any time.

SUMMARY

A case of generalized urticaria following the use of tryparsamide is reported. This reaction occurred on four separate attempts to use this form of therapy.

Clinical Notes

ZINC PEROXIDE IN THE TREATMENT OF DERMATOPHYTOSIS

SAMUEL FELDMAN, M.D., NEW YORK

In the twenty years since the publication of the paper introducing potassium permanganate as a remedy in the treatment of dermatophytosis, by myself in collaboration with the late Dr. Benjamin F. Ochs,[1] the merits and shortcomings of this treatment have become more definitely established.

The greatest drawback to the use of this drug is that it is not stable and that it cannot be combined with any base in the form of either an ointment or a drying lotion. For that reason it is suitable only for a hot soak or a wet dressing, and, naturally, its use is limited to the early acute stage of the disease.

There is one period during the course of the disease when the use of irritating ointments and greases is, to say the least, inadvisable, if not contraindicated, namely, when the acuteness of the lesions has subsided, the blebs have broken and the skin is macerated and exuding. Wet dressings are still helpful in this stage, but patients are not always able to remain away from their usual occupation in order to avail themselves of that method of treatment.

An ideal substitute for potassium permanganate should have a similar therapeutic action and should be available for combination with a suitable base. Zinc peroxide is preeminently suited for that purpose. In the Morrisania City Hospital my associates and I have treated more than 30 patients with ringworm with an ointment of 10 per cent zinc peroxide in a vanishing cream base consisting of a mixture of potassium stearate and potassium palmitate. Gratifying results were obtained. There is a relief of itching in a comparatively short time. Macerated and exuding lesions become dry and clean looking within a few days and usually heal within a few weeks. Treatment with this preparation is a great convenience to the patient because it is not greasy and does not soil footwear and bedclothes. It seems to be of particular value in the treatment of lesions between the fingers and between the toes, even in cases in which fissures are present.

Zinc peroxide is comparatively unstable when sterilized for surgical use, and as far as oxygen liberation is concerned it is essentially impotent after about one month's time. In the unheated state it is fairly stable and, as tests have shown, remains the same for a year or more.

For dermatophytosis a preparation (zinc superoxide, Merck) may be used which consists of 45 per cent zinc peroxide (ZnO_2) and 55 per cent zinc oxide (ZnO). Its oxygen content is 7.4 per cent. This product is more stable than zinc peroxide alone and, furthermore, there is no need of sterilizing it before it is used; hence deterioration from that source is avoided. In contact with moisture, even such quantities as might be present in a vanishing cream base, there would be liberation of oxygen, but in quantities not sufficient to interfere with its therapeutic activity.

1. Feldman, S., and Ochs, B. F.: Potassium Permanganate as a Curative Agent in Dermatologic Diseases, Arch. Dermat. & Syph. **6**:163 (Aug.) 1922.

A suitable vanishing cream base can be made with the following formula: stearic acid U. S. P. (containing quantities of palmitic acid), 20 per cent; glycerin, 3.4 per cent; potassium hydroxide, 1.8 per cent, and water, 80 per cent.

The material for this investigation was furnished by Vogel Laboratories, Lake Mohegan, N. Y., in the form of "superoxide ointment." Laboratory tests of this preparation, made by Bendiner and Schlessinger, New York, July 10, 1941, gave the following results: The average oxygen content of the 10 per cent ointment was 0.74 per cent. One specimen, prepared on January 25, had an oxygen content of 0.73 per cent; another, prepared on February 7, a content of 0.81 per cent, and a third, compounded on June 27, a content of 0.74 per cent. The loss, if any, was negligible. It is evident that the stock ointment is fairly stable. However, it must be kept in a cool place and in a closed jar provided with a nonmetallic cap. Space in the jar must be allowed for an accidental accumulation of oxygen.

When the ointment was spread on a glass slide to a thickness of 3 mm. and exposed in ordinary room temperature, it lost 80 per cent of its oxygen within twenty-four hours. For that reason it is advisable to apply the ointment at least once, and preferably twice, a day in order to obtain an optimum therapeutic effect.

I am not offering a cure for dermatophytosis, but I feel that this remedy deserves a high place among the drugs and preparations now in use.

1955 Grand Concourse.

TINEA VERSICOLOR INVOLVING THE SCALP

RUDOLF L. BAER, M.D., NEW YORK, AND EUGENE S. BERESTON, M.D., BALTIMORE

Several years ago one of us (R. B.) reported a case of tinea versicolor of the scalp.[1] A short review of the literature on the subject was given at that time, and it was stated that the case was the first one to be reported in the American literature. Recently we had the opportunity of observing another case, which presented a clinical picture identical with that seen in the previously reported case.

REPORT OF A CASE

J. G., a white man aged 58, of Russian nativity, was admitted to Montefiore Hospital for Chronic Diseases on April 13, 1941. He was suffering from intramedullary disease, arteriosclerotic and hypertensive heart disease, old fibroid pulmonary tuberculosis and a left hydrocele.

For many years prior to his admission to the hospital the patient had noticed brownish scaly lesions on his trunk; these did not give rise to any symptoms. Exposure of the uncovered scalp to the sun for several hours, shortly after admission, caused a decided erythema. A few days later it was noticed that the major part of the scalp in the parietal and occipital regions had become light pink and that the pink areas were surrounded by a darker brownish zone. The light pink areas were scaly and irregularly shaped and included hairy as well as

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From the Dermatologic Department, service of Dr. Fred Wise, Montefiore Hospital for Chronic Diseases, New York.

1. Baer, R. L.: Tinea Versicolor Involving the Scalp, Arch. Dermat. & Syph. **37**:970 (June) 1938.

bald parts of the scalp. Within this area there were numerous pea-sized, irregularly shaped, brownish yellow macules. The large pink area was surrounded by fairly dark, yellowish brown skin. Fine branny scaling was noticed all over the scalp. The appearance of the pink areas suggested atrophy. The trunk, as well as the arms and the lower part of the buttocks, was covered by an eruption consisting of pinhead-sized to nickel-sized yellowish brown fine scaly areas, which had coalesced in some sites.

Scrapings taken from the scaly areas on the scalp and trunk revealed the typical mycelium and spores of Microsporon furfur.

COMMENT

This is the second case of tinea versicolor involving the scalp which has been described in the American literature. The first case was reported by one of us (R. B.) in 1938. The common features of this case and the first one are: (1) the involvement of the hairy part of the scalp; (2) the clinical picture; (3) the widespread involvement of the body; (4) the fact that both patients were immigrants from Russia, and (5) the fact that both patients were subject to pulmonary tuberculosis.

MATCH DERMATITIS IN AN UNUSUAL LOCATION

H. J. Templeton, M.D., Oakland, Calif.

The possible types and locations of contact dermatitis are almost endless, and it would be impossible to tabulate them all. Because of the unusual location I am reporting the following case of match dermatitis. Only a chance remark by the patient enabled me to recognize the offending agent, which I certainly never would have suspected.

REPORT OF A CASE

F. Z., a man aged 44, a ship's officer, came to me on May 8, 1941 because of extremely acute dermatitis of the ears, including the aural canals. He had had a number of similar attacks in the previous three years.

Because of the fact that he wore radio headphones and came in frequent contact with cement dust I suspected these substances. But patch tests with them elicited negative reactions. The offending agent came to light when the patient remarked: "The itching is so intense that I have to scratch deep into the ear canals with matches." A patch test with his matches elicited a strongly positive reaction (vesiculation), and recovery followed avoidance of them.

Submitted for publication, June 23, 1941.

News and Comment

AMERICAN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Applications are now being received for places on the program of the Section on Dermatology and Syphilology of the American Medical Association for the meeting to be held at Atlantic City, N. J., June 8 to 12, 1942. All Fellows of the American Medical Association are eligible. Essayists who are not Fellows may be accepted by invitation. The program is usually assembled in the early part of December.

All applications should be addressed to Dr. Nelson Paul Anderson, Secretary of the Section on Dermatology and Syphilology, 2007 Wilshire Boulevard, Los Angeles.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

NECROBIOSIS LIPOIDICA DIABETICORUM. ALICE HILDEBRAND, HAMILTON MONTGOMERY and EDWARD RYNEARSON, Arch. Int. Med. **66**:851 (Oct.) 1940.

Hildebrand and her associates review the reports of 78 instances of necrobiosis lipoidica diabeticorum and add their observations in 8 cases discovered among a total of 2,000 diabetic patients. Nearly 90 per cent of these patients had diabetes mellitus; 80 per cent were women. This disease is primarily one of young persons. Trauma was thought to play a role in the development of the disease in about 15 per cent of the patients.

Clinical and microscopic observations of the authors' 8 patients are reported in detail. Quantitative determinations of the lipoid constituents of the lesions were suggestive of a relative increase of lecithin in the tissues. It is pointed out that in the majority of all reported cases the blood lipoids were within normal limits. The pathogenesis of the disease remains obscure.

CASTRATION OF THE MALE. ROBERT C. MOEHLIG, Endocrinology **27**:743 (Nov.) 1940.

Moehlig submits reports of 2 instances of castration in the male. In the first case almost complete alopecia was noted two years after castration. After repeated injections of testosterone propionate, there was regrowth of hair on the face as well as on the scalp. The second patient was given no therapy but there was complete loss of hair except for a sparse growth over the pubis.

LYNCH, St. Paul.

HAVERHILLIA MULTIFORMIS SEPTICEMIA: ITS ETIOLOGIC AND CLINICAL RELATIONSHIP TO HAVERHILL AND RAT BITE FEVERS. F. F. ALLBRITTEN, R. F. SHEELY and W. A. JEFFERS, J. A. M. A. **114**:2360 (June 15) 1940.

Allbritten, Sheely and Jeffers report the case of a man aged 21 in whom the bite of a white rat was followed three days later by malaise, a chill and a resultant fever with an initial temperature of 105 F. In the first examination the patient was noted to be somewhat disorientated; there was slight congestion of the mucous membranes of the throat and eyelids, and there was moderate generalized involvement of the lymph nodes. The white blood cell count showed 32,000 cells. On the second day of the illness a rash appeared on the trunk, consisting of discrete maculopapules. They faded after four days. During a second paroxysm a similar eruption was noted, but this time the lesions were confluent and were present on the extremities. On the tenth day several tender nodules appeared on the finger tips. The next day these became purpuric, and later yellow unbilicated centers developed. The histologic section showed a nonspecific inflammatory reaction. There were also many small petechial and purpuric spots over the lateral aspects of the feet. Many of the joints became swollen and painful. Treatment consisted of the administration of potassium iodide, a blood transfusion and the injection of neoarsphenamine. No spirilla forms were found on direct mounts or in examination of animals inoculated with samples of blood. Cultures of the blood revealed Haverhillia multiformis. Intraperitoneal inoculation of a white mouse with the organisms cultured on broth caused polyarthritis and other characteristic lesions.

EXTRAGENITAL TRANSMISSION OF SYPHILIS AMONG FIVE PERSONS IN ONE FAMILY. G. R. ROWNTREE and J. R. HENDON, J. A. M. A. **115**:117 (July 13) 1940.

After the initial visit in which syphilis was discovered in a patient, Rowntree and Hendon found the disease in 4 other persons in a household of 11 members. The initial lesion was extragenital in all 5 instances.

A CONVENIENT METHOD OF APPLYING WET DRESSINGS. G. V. STRYKER and J. GRINDON JR., J. A. M. A. **115**:121 (July 13) 1940.

Stryker and Grindon describe a simple and effective method of applying continuous wet dressings to the hands and feet. They have found that mitts or socks made of pliofilm are moisture proof, oil proof, odorless, nonirritating, pliable, thin, durable, tear resistant, sewable, heat sealing, not uncomfortably warm, noninflammable, resistant to weak acid and alkali and inexpensive.

SYPHILIS OF THE BONES IN INFANCY: SOME POSSIBLE ERRORS IN THE ROENTGEN DIAGNOSIS. W. A. EVANS, J. A. M. A. **115**:197 (July 20) 1940.

Evans cites cases to illustrate the difficulty often encountered in the diagnosis of congenital syphilis. The roentgen examination of the bones may not show positive evidence of the disease for several weeks after birth. Periosteal shadows are not considered by Evans as pathognomonic of syphilis in the absence of other manifestations, since they may also occur in subperiosteal fractures occurring at delivery, in rickets, in tuberculosis and in other forms of osteomyelitis, and often the cause is obscure.

POSTARSPHENAMINE JAUNDICE APPARENTLY DUE TO OBSTRUCTION OF INTRAHEPATIC BILIARY TRACT. F. M. HANGER JR. and A. B. GUTMAN, J. A. M. A. **115**:263 (July 27) 1940.

Hanger and Gutman report the cases of 12 patients in whom postarsphenamine jaundice developed which was considered due to obstruction of the intrahepatic biliary tract. Constitutional and gastrointestinal symptoms appeared after the second or third arsenical injection. Jaundice developed after several days and persisted for weeks or months. There was no evidence of degeneration in the liver. The patients all recovered.

DERMATITIS FOLLOWING THE WEARING OF NYLON STOCKINGS: PRELIMINARY REPORT OF FOUR CASES. S. J. FANBURG, J. A. M. A. **115**:354 (Aug. 3) 1940.

In 4 instances of dermatitis of the legs and thighs, Fanburg proved by patch tests that the cause was a dye or finish used in preparing nylon stockings.

USE OF BISMUTH INJECTIONS TO MANAGE COURSE OF THERAPEUTIC MALARIA. H. N. COLE, G. A. DEOREO, J. R. DRIVER, H. H. JOHNSON and W. F. SCHWARTZ, J. A. M. A. **115**:422 (Aug. 10) 1940.

Cole, DeOreo, Driver, Johnson and Schwartz advocate the use of bismuth, preferably thio-bismol, to stop temporarily the course of malarial chills when alarming symptoms develop. One to three day rest periods from the chills allow the patient to recover sufficiently so that further chills may then be allowed. With the use of thio-bismol in 263 cases of therapeutic malaria, the death rate was 2.24 per cent, as compared with a previously reported mortality rate in similar cases of 7.51 per cent. Bismuth is not advocated as a substitute for quinine when it is desired to terminate malaria, but when this substance is used in conjunction with quinine the fever is terminated without shock to the patient.

HISTAMINASE IN THE TREATMENT OF ALLERGIC DERMATOSES. L. C. GOLDBERG, J. A. M. A. **115**:429 (Aug. 10) 1940.

From his experience with the use of histaminase in 35 cases, Goldberg found the substance useful in the treatment of certain allergic dermatoses. Only 9 patients were unimproved. The diseases treated included papular urticaria, atopic dermatitis, chronic urticaria and idiopathic pruritus. Histaminase was used both orally and by injection. Patients receiving intramuscular injections of histaminase had better results than those who received the enzyme in tablet form.

CHRONIC CONJUNCTIVITIS DUE TO THE VIRUS OF VENEREAL LYMPHOGRANULOMA. W. CURTH, H. O. CURTH and M. SANDERS, J. A. M. A. **115**:445 (Aug. 10) 1940.

Curth, Curth and Sanders report a case of chronic conjunctivitis in which the cause was determined to be the virus of venereal lymphogranuloma; the patient was studied six years after the infection had been acquired. The virus was grown in tissue cultures, and by intradermal tests in patients it was demonstrated in an extract of tissue. Treatment by sulfanilamide was effective in reducing the activity of the process; vision had been lost several years before.

OCCUPATIONAL DERMATITIS FROM HANDLING RESIN-LINED TIN CANS. L. SCHWARTZ and J. P. RUSSELL, J. A. M. A. **115**:448 (Aug. 10) 1940.

Schwartz and Russell observed cases of dermatitis affecting principally the cubital spaces and axillas in workers handling new tin cans. Metallic colored dust was found in places where the cans were deposited and when used in patch tests was found capable of eliciting reactions in some of the patients. Besides tin and iron, the dust contained a resin, the exact composition of which could not be determined. The resin was used to line the tin cans and was considered by the authors to be the cause of the dermatitis.

LEWIS, New York.

THE PLACENTAL TRANSMISSION OF ANTIBODIES IN THE SKIN SENSITIVE TYPE OF HUMAN ALLERGY. WILLIAM B. SHERMAN, STANLEY F. HAMPTON and ROBERT A. COOKE, J. Exper. Med. **27**:611 (Nov.) 1940.

The authors report that a comparison of 12 maternal and 12 corresponding cord serums by the method of passive transfer showed the human placenta to be impermeable to skin-sensitizing antibodies. Direct cutaneous tests and passive transfer studies of 6 infants at the ages of 3 to 6 months showed negative reactions to the antigens to which their mothers were sensitive.

By these reactions there is demonstrated a difference between skin-sensitizing antibodies and the blocking antibody present in the serums of patients with hay fever, hemagglutinins and typhoid agglutinins, the placenta being permeable to the latter substances.

LYNCH, St. Paul.

CANCER OF THE SKIN. HENRY MACCORMAC, Brit. J. Dermat. **52**:141 (May) 1940.

MacCormac is of the opinion that the progress and treatment of an epithelioma depend more on its site of origin than on its microscopic architecture. The heightened malignancy of growths on the mucous membrane as compared with those on the skin is accounted for by the more active blood and lymph supply and the greater mobility of the mucous surfaces. He questions the justification of a cleancut division of epitheliomas into basal and prickle cell types on clinical or pathologic grounds. Occasionally basal cell types show capricious behavior, and they are difficult to explain if one adheres strictly to two separate and distinct forms of cutaneous cancer, whereas no difference arises if one presumes there is only one form, the predominating cellular type being an expression of rate of growth rather than an indication of the layer of the epidermis from which the tumor originated.

A Case of Pili Torti. F. F. Hellier, W. T. Astbury and Florence O. Bell, Brit. J. Dermat. **52**:173 (June) 1940.

This case is apparently the first one of its kind to be described in England. In all, about 30 cases of pili torti have been referred to in the literature. The condition resembles monilethrix, but on microscopic examination the hairs are not beaded but flattened and at irregular intervals completely twisted through 180 degrees around the long axis. Clinically there is a peculiar spangled glint due to the unequal reflection of light from the twisted hair. The majority of the affected children are born without hair, and the lesion appears only with the growth of hair, which is frequently delayed till the age of 2 years. Girls are affected more than boys, and heredity plays some part in the condition. In the case reported there was also considerable keratosis pilaris. The prognosis is rather favorable. In this case epilation with thallium acetate was followed by considerable improvement.

A roentgen ray diffraction study, which is concerned with molecular structure, indicated that "neither pili torti nor monilethrix involves any molecular disturbance recognizable by X-ray diffraction as a departure from the familiar keratin type of structure; though the anomalies must be traceable ultimately to molecular causes, they manifest themselves rather as histological irregularities."

Sudden Death in Infantile Eczema. J. H. Twiston Davies, Brit. J. Dermat. **52**:182 (June) 1940.

The author reports 3 cases of this redoubtable complication in order to discourage light-hearted hospitalization. In similar cases previously reported death has been attributed to cross infection, status thymicolymphaticus and anaphylactic shock. None of these conditions apparently played a role in the cases reported. In cases of this kind death occurs, as a rule, within a few days after separation of the child from the mother and irrespective of treatment, nursing or nutrition. The author hints that perhaps psychologic disturbances may play a causative role. He poses the question: "Can it be that the eczema in an infant is perhaps compensated by certain profound systemic and humoral adjustments, and that sudden removal of both the psychological stimulus and the eczema itself leads to a fatal upsetting of this balance?" In 2 of the cases reported it was clear that the mother did not particularly want the child.

Some Observations on Intracutaneous Reactions in Allergic Eczemas. H. Haxthausen, Brit. J. Dermat. **52**:191 (June) 1940.

Haxthausen maintains that supersensitiveness in eczemas is often found in the corium as well as in the epidermis. He has found that intracutaneous injections with solutions of nickel, chromium and mercury have elicited positive late reactions in the form of red infiltrated papules which persist for several days. In some of the cases, after the appearance of the positive intracutaneous reaction, peculiar pseudopodia-like excrescences extend from the papule as tortuous red streaks, which apparently represent an inflammatory process spreading along the lymphatics of the skin. He suggests that perhaps this reaction may be due to a secretory product which keeps on being produced for a considerable length of time and that if research is successful in isolating this hypothetic substance it will be of importance in explaining the eczematous reactions. Haxthausen has the opinion that it is not justifiable to maintain a sharp distinction between the two forms of allergy, epidermal hypersensitiveness and hypersensitiveness in the corium. He says that in most cases of allergic eczema the corium is probably involved in the hypersensitiveness. In practice, under ordinary conditions, only the epidermis is exposed to the antigen.

Rattner, Chicago.

PURE RECTAL STENOSIS IN LYMPHOGRANULOMA VENEREUM. J. A. URQUIZO and A. E. DESPONTÍN, Rev. méd. latino-am. **25**:1346 (Sept.) 1940.

The authors present 2 cases of lymphogranulomatous rectal stenosis and on the basis of thorough studies suggest that these should truly be termed cases of stenosing rectosigmoideocolitis. They believe that the natural tendency of the infiltrative process is to ascend to the upper regions of the bowel during the evolutionary phase of the disease and observed such involvement by sigmoidoscopic and roentgenographic examinations. In cases in which the intradermal Frei reaction is negative the authors employ the intravenous route (hemoreaction of Ravaut). They prefer the human antigen. In every suspected case they recommend early rectal examination, since the best therapeutic results are obtained in the earlier stages of the disease. Depending on the degree of intestinal involvement, they recommend a left-sided colostomy in the earlier stages, a resection of the bowel in the later stages and of course immediate colostomy when acute intestinal obstructions are present. Medical treatment, such as local topical applications and the administration of sulfanilamide and its derivatives, is considered helpful adjuvant therapy.

LEIFER, New York.

SYMPTOMS AND ETIOLOGY OF CONGENITAL ECTODERMAL DYSPLASIA. K. J. BORGGREVE and I. COHEN, Dermatologica **82**:25, 1940.

A boy, an only child, showed the typical syndrome of congenital ectodermal dysplasia with anhidrosis, hypotrichosis and deficient dentition. Histologic examination of skin from the back showed normal skin without sweat glands, sebaceous glands or follicles. The boy had attacks of fever, which may be explained by a lack of thermic regulation; they could be reproduced by exposure to an arc lamp. The boy suffered frequently from eczema. A cousin had a congenital cataract. The Wassermann, Sachs-Georgi, Kahn, Meinicke and citochol reactions were negative. His maternal grandmother had acquired syphilis after the birth of her fourth child. The mother, who was the sixth child, and 2 of her sisters had congenital syphilis but no ectodermal dysplasia. Fournier's "parasyphilis" may be of etiologic significance in this case.

HELEN O. CURTH, New York.

INFANTILE ACRODYNIA AND ENCEPHALITIS. B. DYKSTRA, Maandschr. v. kindergeneesk. **9**:292 (April) 1940.

A case of infantile acrodynia in a girl of 4¼ years is described. Her illness was regarded as due to encephalitis, in view of the motor disturbances, the vegetative derangement of central origin and the abnormal composition of the cerebrospinal fluid. In connection with etiology, Debré's theory of alimentary intoxication and the theory of infection by Kuiper, Selter, Boureé and others are briefly discussed. The author concludes that the infective theory is to be preferred at present. Accordingly, infantile acrodynia is regarded as a disease caused by a separate neurotripic virus. Finally, the importance of the study of factors which increase the predisposition is stressed.

VAN CREVELD, Amsterdam, Netherlands. [AM. J. DIS. CHILD.]

REGRESSION OF PULMONARY MANIFESTATIONS IN A CASE OF BENIGN LYMPHOGRANULOMATOSIS FOLLOWING AN ATTACK OF ERYTHEMA NODOSUM. G. BOSTROM, Acta dermat.-venereol. **21**:38 (Feb.) 1940.

The author discusses the cause of lymphogranulomatosis benigna and describes a case with typical changes in the lungs and swelling of the cervical lymph glands. The patient had a typical eruption of erythema nodosum. About six months later this patient was reexamined roentgenologically. The infiltration in the lungs had almost completely cleared up. At the same time the reaction to tuberculin, which had been negative at first, became strongly positive.

THE USE OF BLOOD TRANSFUSIONS IN CASES OF DERMATOSES. A. BUSCHKE, Acta dermat.-venereol. **21**:53 (Feb.) 1940.

The author discusses the question of the value of blood transfusions in the treatment of cutaneous diseases and cites the literature on this subject. He describes an unusual case of pustular psoriasis accompanied by an extensive and grave dermatitis. The patient did not respond to any kind of therapy but improved as a result of several blood transfusions.

Theories as to the action of transfusions in cases of dermatoses are discussed.

HERPES ZOSTER GENERALISATUS AND LYMPHATIC LEUKEMIA. B. BAFVERSTEDT, Acta dermat.-venereol. **21**:60 (Feb.) 1940.

The author discusses the relation between generalized herpes zoster and various forms of lymphoblastomas and claims that 60 per cent of herpes zoster eruptions which appear in combination with leukemia are generalized in character. A case of hemorrhagic zoster accompanied by a generalized varicella-like eruption is described. The patient was also suffering from lymphatic leukemia.

The author stresses the importance of general physical examination, including a blood count, in cases of generalized herpes zoster. The question of the relation between herpes zoster and varicella is discussed.

SIMULTANEOUS OCCURRENCE OF LYMPHOGRANULOMA VENEREUM AND CHANCROID. H. ENGELSON, Acta dermat.-venereol. **21**:118 (Feb.) 1940.

The author cites the case of a patient in whom a penile ulceration developed five days after sexual intercourse. Five weeks later a painful swelling of the inguinal lymph glands developed, followed by suppuration and perforation. A swelling on the neck followed by perforation and purulent discharge appeared several days later. The intradermal injection of the Ito-Reenstierna antigen elicited a positive reaction twice. The reaction to a Frei test was also positive. The intradermal injection of an antigen prepared from the pus obtained from the lesion on the patient's neck also elicited a positive reaction.

LYMPHOGRANULOMA INGUINALE FROM AN IMMUNOBIOLOGICAL POINT OF VIEW. SVEN HELLERSTROM, Acta dermat.-venereol. **21**:222 (Feb.) 1940.

Lymphogranuloma venereum is considerably more common than was formerly assumed. The Frei test has proved to be as reliable and specific as can be expected of any biologic test. The author describes the technic of the test, the various strengths of the antigen, the length of time between the infection and the development of cutaneous allergy and its duration. He also discusses the influence of mixed infections and mentions the fact that florid syphilis may exert a preventive or repressive influence on the reaction for lymphogranuloma venereum. The author stresses the fact that a negative Frei reaction even over a long period does not exclude the presence of lymphogranuloma venereum; the testing must be continued. The relation between erythema nodosum and lymphogranuloma venereum is discussed. The author cites Kornblith in saying that the Frei antigen given intravenously was found to be the most useful single method of therapy. Elevation of temperature and a decided leukopenia follow these intravenous injections. The author also mentions the fact that surgical extirpation of one affected lymph gland has a favorable therapeutic effect on the remaining lymph glands. The author believes that surgical intervention induces an unusually strong "intravenous Frei reaction" with the aforementioned favorable therapeutic effect.

The question of transferring the virus of lymphogranuloma venereum from animals to man and from one person to another is also discussed.

ASTRACHAN, New York.

Society Transactions

DERMATOLOGICAL CONFERENCE OF THE MISSISSIPPI VALLEY AND CENTRAL STATES DERMATOLOGICAL ASSOCIATION

DR. ELMORE B. TAUBER, *Presiding*

Joint Meeting, Cincinnati, Feb. 9, 1941

All the presentations were made by members of the Cincinnati Society of Dermatology and Syphilology.

Papulonecrotic Tuberculid.

The patient, a woman aged 31, has had a disease of the skin since 1936. She began to menstruate every six weeks when she was 12 years old and so continued until she was 20. At that time, 1930, she began to menstruate only once every two or three months and to gain weight, going from 103 pounds (46.7 Kg.) in 1930 to 170 pounds (77 Kg.) in 1936. In 1933 she took dinitrophenol to reduce her weight. In 1936 she took chorionic gonadotropin (antuitrin S) and thyroid, lost weight to 111 pounds (50.3 Kg.) and began to menstruate every six weeks. At about the same time an eruption appeared, which has persisted to date. The first lesions appeared on the knees and elbows. The lesions are always similar, beginning as papules with slight redness; then a mass becomes palpable below the papule; the latter becomes crusted, and when the crust falls a depressed scar remains. The whole cycle is completed in two or three weeks. There are no subjective symptoms. Two years ago lesions appeared on the skin over the joints of the index fingers. In the summer of 1939 she had a severe attack of poison ivy dermatitis, but it did not seem to influence her other eruption. The eruption is better in winter and worse in summer. For the past year lesions have appeared on the face, shoulders, forearms, back, waistline, thighs, legs and dorsa of the feet. There have been none on the scalp, neck, palms, buttocks, popliteal region, toes or soles. There is no discomfort unless the lesions are traumatized. She tires easily but has no afternoon fever, night sweats, cough, pain in the chest or hemoptysis.

A paternal aunt died of Hodgkin's disease. The patient has had frequent discomfort in the throat, near the base of the neck. An abscess of the right eyeball was lanced when she was 5 years old.

On the knees, elbows, lower part of the upper arms posteriorly and lower part of the thighs anteriorly are grouped, discrete white depressed atrophic scars and pigmented depressed lesions, each measuring about 5 mm. in diameter. A few similar lesions are scattered over the back and over the posterior and lateral aspects of the thighs. Isolated lesions are noted on the right cheek, under the chin, on the left lateral aspect of the nose and on the left shoulder anteriorly. One firm red papule is noted on the right knee, and there are a few scaly red papular lesions on the elbows.

The remainder of the physical examination showed no abnormalities.

The Kahn reaction was negative. The blood count and the urine were normal. Histologic examination showed nothing characteristic of tuberculosis. Roentgenograms of the chest were normal.

DISCUSSION

DR. KARL G. ZWICK, Cincinnati: The patient's statements as to seasonal recrudescences are in accord with the description of the papulonecrotic tuberculid in textbooks, but the note in the patient's history that "the condition is better in

winter and worse in summer" contradicts my observations. As no tuberculin tests were made, a valuable diagnostic aid is lacking. Although Koch's organisms are generally absent or present only in limited numbers in the papulonecrotic tuberculid, the reaction to a tuberculin test is frequently strongly positive, indicating a hyperergic state.

DR. ELMORE B. TAUBER, Cincinnati: The patient made that statement about seasonal involvement today for the first time. When I questioned her she said the eruption occurred in showers in the summer just as in the winter, but she did not think it was as bad in the winter.

DR. NORMAN TOBIAS, St. Louis: In regard to roentgenograms of the chest, in my experience quiescent hilar gland tuberculosis is common in cases of papulonecrotic tuberculid.

DR. SAMUEL GOLDBLATT, Cincinnati: The patient gave a definite history of having taken for years laxative tablets the essential ingredient of which is aloe and also a laxative containing phenolphthalein.

Sarcoid, with Postencephalitic Parkinsonism.

The patient, a white woman aged 48, was in general good health except for "nervousness" until four years ago, when the skin on the right side of the bridge of the nose broke down as a result of irritation from the rim of her glasses. It healed in four or five days, but approximately a year later it again broke down; it healed gradually, leaving a scar. Each episode occurred while she was wearing glasses. About Nov. 1, 1940 a raised reddened patch, tender to palpation, developed in the same area.

Her right eye has been "sore and watery" for twenty years; at times pus appears at the inner angle. She gives a history of nervousness and tremor for the past twenty-six years. On November 19 neurologic diagnosis was parkinsonism, probably postencephalitic. There is no family history of tuberculosis or disease of the skin.

On the right side of the bridge of the nose is an oval, flat, slightly elevated smooth plaque, the lower half of which is dark red while the upper half is yellowish brown. There is one area of atrophy, about 2 mm. in diameter. A few telangiectases are noted at the periphery. There are depigmented white spots on the abdomen, left wrist and back of the neck.

The Kahn reaction was negative. The blood count and urine were normal. Roentgenograms of the chest and of the hands were normal. The reaction to a tuberculin test was negative.

Histologic examination showed collections of epithelioid cells and scattered giant cells.

Treatment has consisted of the administration of a bismuth compound, 2 cc. weekly, sulfanilamide, 2 grains (0.13 Gm.) four times a day, and quinine and zinc oxide ointment locally. With this treatment the lesion appears unchanged, although the tenderness has gone.

Sarcoid (Darier-Roussy).

At the age of 12 years the patient, a white man now aged 49, suffered a severe abrasion of the right leg, which healed with a scar. There was no further trouble until 1918, at the age of 26, when he was badly cut in the region of the scar. A chronic "sore" developed, which was progressive, involving almost the whole right leg. There has been rather frequent ulceration. It has caused no symptoms.

The patient was "gassed" during the World War (1918) and since then has had a chronic asthmatic condition. He has frequent colds and bronchitis. In 1922 he coughed up a slight amount of blood. One specimen of sputum at this time showed tubercle bacilli, but subsequent examinations showed none. Roentgenograms of the chest have been normal.

There is some increase in the size of the right leg. Involving all aspects of the leg from knee to ankle is a diffuse induration of the skin; the skin of the upper third is red and smooth, and on the lower two thirds there is a slightly elevated firm infiltration, the surface of which is irregular and violaceous. There is a punched-out ulcer, about 2.5 cm. in diameter, in the upper part of this area, while a similar ulcer about 1 cm. in diameter is located in the middle of its posterior aspect.

The eyes, nose and throat show evidence of an acute infection of the upper respiratory tract. Dry rales are heard throughout both pulmonary fields. Spider nevi are present on the upper part of the abdomen.

The Kahn reaction was negative, and urine was normal. The result of a tuberculin patch test with purified protein derivative no. 1 was negative on both the forearm and the right leg. A blood count showed 5,500,000 red cells and 10,000 white cells. The hemoglobin amounted to 15..4 Gm. per hundred cubic centimeters.

Histologic examination of material from the upper border of the lesion showed some atrophy of the epidermis, a collection of epithelioid cells in one portion of the slide with epithelioid infiltrate extending deep through the cutis and into the subcutaneous tissue and a relatively large number of giant cells scattered throughout the section. The vessel walls were thickened. Collagenous tissue bundles showed increased thickness and edema. Staining for acid-fast organisms gave negative results.

Therapy consisted of local application of phenolated petrolatum locally, and a vitamin A and D compound internally. No improvement followed this management.

DISCUSSION OF CASES OF SARCOID

DR. I. J. ARNSSON, Buffalo: I think clinically as well as histologically the condition in the second case is tuberculoid syphilis and not sarcoid. The histologic picture shows definite proliferations of the intima of the blood vessels, such as one finds in syphilis and not in tuberculosis. The patient stated that during the war while he was in France on one occasion his Wassermann reaction was positive. He is not married.

DR. ELMORE B. TAUBER, Cincinnati: I thought the picture would fit in with sarcoid of Darier and Roussy, but there was also a possibility of syphilis.

DR. HARRY CLAASSEN, Cincinnati: This man has had this condition for twenty-two years, which should rule out syphilis, as this disease does in months what tuberculosis does in years. Secondly, the lesion has none of the characteristics of an ulcerating nodular syphiloderm. There is no serpiginous bluish red nodular border with the scarred center. Histologically it is difficult to distinguish between syphilis and tuberculosis.

Lichen Nitidus in a Negro Child.

The patient is a Negro boy aged 7 years. In 1937, shortly after an appendectomy and reduction of an intussusception, small bumps were noted on the elbows and on the knees. The lesions were pruritic. His general condition has been good. There is no history of chorea. There is no familial history of tuebrculosis.

In the posterior cervical region, on the elbows, knees and flexor surfaces of the wrists and forearms, in the popliteal space and on the penis are many discrete small, light brown firm papules. In many areas of the trunk there are small follicular plugs. There is no generalized glandular enlargement.

The Kahn reaction was negative. A roentgenogram of the chest showed that the markings in the right lung and in the base of the left lung were increased slightly but no infiltrate was present. A tuberculin test with purified protein derivative no. 1 elicited a positive reaction.

Histologic examination showed dense lymphocytic and epithelioid cell infiltrate and perivascular lymphocytic infiltrate.

Mild keratolytic ointments have been employed. In the past three months of observation the lesions have spread gradually.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I agree with the diagnosis of lichen nitidus. I was interested in the linear arrangement of many of the lesions.

DR. ELMORE B. TAUBER, Cincinnati: I think linear lesions occur occasionally.

DR. LOREN W. SHAFFER, Detroit: I suggest that the question of vitamin deficiency be investigated. The lesions on the back of the neck are suggestive of vitamin A deficiency. A biopsy would settle the question.

DR. B. F. BARNEY, Columbus, Ohio: I have the same idea. In an article by Brunsting and Sheard (Dark Adaptation in Pityriasis Rubra Pilaris, ARCH. DERMAT. & SYPH. **43**:42 [Jan.] 1941) it was suggested that a condition of this kind might be a tuberculid or a manifestation of vitamin A deficiency.

DR. EARL W. NETHERTON, Cleveland: A biopsy was performed, and I thought the histologic picture, as well as the clinical picture, was characteristic of lichen nitidus. There was a small area of granulomatous infiltration at the peak of one papilla.

DR. KARL G. ZWICK, Cincinnati: The appearance of some of the microscopic sections of the lesions would seem to warrant the consideration of a lichenoid or licheniform tuberculid. The positive tuberculin reaction and the roentgen ray findings in the chest, although the latter are somewhat vague, seem to point in the same direction. However, as Darier (Précis de dermatologie, ed. 4, Paris, Masson & Cie, 1928), Niles (ARCH. DERMAT. & SYPH. **22**:687 [Oct.] 1930) and Ellis and Hill (ibid. **38**:569 [Oct.] 1938) were at times puzzled by the problem of the lichen nitidus, I shall not feel embarrassed if further observations contradict my impression. In regard to the suggestion to link up the condition with a vitamin inadequacy, I can say only that the patient's lesions differ from those which have been brought to my attention as cutaneous manifestations of vitamin deficiencies. But I admit that I have much to learn about the cutaneous signs of dysvitaminoses and avitaminoses.

Hypertrophic Lupus Vulgaris.

J. R., a white man aged 28, states that he has had an eruption on the buttocks for twenty-seven years. It has progressed from a small palm-sized lesion to one which involves the entire buttocks, the crural areas and the upper posterior parts of the thighs. There have been no night sweats, expectoration of blood or loss of weight, and there is no family history of tuberculosis.

He presents a definite brownish red, hypertrophic, verrucoid and scaling nodular, infiltrative eruption which involves the entire buttocks, the upper posterior parts of the thighs, part of the perineal and crural areas and the entire perianal region. In places the eruption is discrete and in others confluent, but all the lesions are in plaque and serpiginous formations. Diascopic examination shows definite "apple jelly" nodules.

The Wassermann and Kahn reactions of the blood were negative. Tests with purified protein derivative in dilutions of 1:100,000 and 1:10,000 elicited negative results. A roentgenogram of the chest showed no active tuberculous changes.

Histologic examination showed hyperkeratosis, acanthosis, diffuse and globular monocytic infiltration, occasional giant cells and numerous epithelioid cells. A Ziehl-Neelsen stain showed no tubercle bacilli.

For its nonspecific effect 0.3 Gm. of neoarsphenamine was given weekly. Also 0.2 to 0.4 cc. of a 15 per cent aqueous solution of starch U. S. P. (corn starch) was injected into various sites along the periphery of this widespread eruption. After

four months of treatment, during which time he received fourteen injections of neoarsphenamine and about fifty-four injections of the starch solution, the area involved has improved about 35 per cent and the patient has gained 6 pounds (2.7 Kg.).

DISCUSSION

DR. ROY L. KILE, Cincinnati: I have been particularly interested in this case and in others of lupus vulgaris in which the treatment has included injections of suspensions of starch. For many years different compounds have been suggested for injection into the nodules of lupus vulgaris for their therapeutic effect (esters of chaulmoogra oil, croton oil, etc.). Many patients have been treated by the injection of starch U. S. P. (corn starch) since my report three years ago (ARCH. DERMAT. & SYPH. **39**:471 [March] 1939). Most of the results have been favorable, and many requests have been received regarding the preparation of the material. The Merrell Drug Company through its research department has made up some of the material in ampules for general use for any one who wants to try it. It has also been suggested to me that the acetate of starch be tried, as it is water soluble and hence would be much easier to handle. The company has also made up some of this for investigational use by any one interested. The products resulting from its breakdown are the same as from ordinary corn starch, and hence it deserves a trial, as it stays readily in solution.

DR. H. J. PARKHURST, Toledo, Ohio: I thought the clinical picture in this case was that of tuberculosis verrucosa cutis rather than of lupus vulgaris.

DR. KARL G. ZWICK, Cincinnati: In view of the improvement in this case credited to treatment with solution of starch, it would interest me to learn the chemical composition (formula) of the starch acetate which was just mentioned.

DR. ELMORE B. TAUBER, Cincinnati: If this patient had been seen before the injections of starch solution were made, the diagnosis of hypertrophic lupus vulgaris would have been substantiated by the majority here. Of course tuberculosis verrucosa cutis was considered. In certain parts the lesion has healed so much that it is really remarkable.

DR. LAWRENCE C. GOLDBERG, Cincinnati: I am going to add an anesthetic to the starch solution so that injection will not be so painful. Injecting the starch solution into the periphery is difficult.

Lichen Nitidus (Generalized).

Mrs. D. M. H., aged 25, was first seen on Jan. 23, 1939. She had experienced repeated attacks of asthma since the age of 2 years and had an eczematoid eruption on the scalp, on the neck, on the face and in the cubital and popliteal spaces for eight years. One and one-half years before consultation a generalized rash developed, which has persisted.

Examination shows seborrhoea capitis, typical atopic dermatitis of the face, neck and cubital and popliteal spaces, with oozing and edema, and generalized pinpoint-sized to pinhead-sized flesh-colored to red papules, some flat topped and shiny and all closely set.

The Wassermann and Kahn reactions of the blood were negative. The urine was normal. The reaction to a test with purified protein derivative (first strength solution) was 3 plus. Intradermal tests with feathers, house dust, corn, oats and wool elicited positive reactions.

The histologic picture of the small shiny papules was that of lichen nitidus, but the structure so closely simulated that of tuberculosis that lichen scrofulosorum and a generalized tuberculosis cutis follicularis disseminatus must be ruled out.

The scalp cleared with the application of sulfur and salicylic acid. The neurodermatitis cleared when the aforementioned allergens were avoided and a mild coal tar preparation was used. It recurred twice with the reinclusion of corn in the diet. The asthma disappeared when the aforementioned inhalants were avoided. A gold compound, a bismuth compound and large doses of vitamins A and D

taken internally and vitamin D applied locally failed to change the lesions of lichen nitidus. Slight improvement occurred recently after repeated injections of tuberculin.

DISCUSSION

DR. B. F. BARNEY, Columbus, Ohio: Unfortunately I did not see the microscopic slide, but the case clinically interested me because recently I have seen 3 patients, 2 of them Negroes, with conditions which I diagnosed as lichen planopilaris. With bismuth therapy the skin cleared up rapidly.

DR. ASHTON L. WELSH, Cincinnati: The histologic picture was that of lichen nitidus except that the infiltrate was heavy and there was much tuberculoid reaction. These findings suggested lichen scrofulosorum or tuberculosis cutis follicularis disseminatus. She has recently received small doses of tuberculin intradermally and has improved greatly. She also has an atopic eczema, which complicates the picture. The areas on the flexor surface of the arms are somewhat modified by the eczema. Typical lesions are present today in the popliteal and cubital areas. The case was of interest because of the complete generalization of the lichen nitidus. The possibility that her atopic state may have accounted for this generalization might warrant some consideration.

DR. G. H. CURTIS, Cleveland: I noticed in the reports of the 2 cases presented that superficial roentgen therapy had not been mentioned. Recently Dr. Netherton and I had 2 patients with lichen nitidus; one was a white woman and the other was a Negro man. The diagnosis was definitely confirmed by the histologic picture. Seventy-five r of unfiltered roentgen rays of low voltage at weekly intervals for five weeks caused the lesions on the woman to disappear. As an experiment in the case of the Negro, half of the cutaneous surface was treated with a keratolytic ointment and the other half with unfiltered low voltage roentgen rays. After five weeks of treatment, the lesions treated with the ointment seemed unaffected, while those treated with roentgen rays had practically disappeared.

DR. ASHTON L. WELSH, Cincinnati: This patient had roentgen ray therapy to three test areas, with no response.

Cutis Verticis Gyrata of the Acromegalic Type.

G. B., a farmer aged 58, with an irrelevant past history, enjoyed good health until 1906, when suddenly his features began to change and his legs, feet, hands and head seemed to grow larger. This excessive growth continued for about one year; then it stopped, and there has been no change in his appearance since that time. The patient's general health since then has been good with the exception of some slight weakness and some difficulty in walking due to the size and clumsiness of his lower extremities.

The patient presents the typical features of comparatively mild acromegaly. In particular he presents one feature of acromegaly which is not usually seen, namely, an extreme furrowing of the skin of the scalp and forehead.

A roentgenogram of the skull showed no abnormalities of the sella turcica.

DISCUSSION

DR. JAMES W. BAGBY, St. Louis: I noticed that this man also had an epithelioma on the right lower eyelid.

DR. ELMORE B. TAUBER, Cincinnati: There are many seborrheic and melanotic lesions that look as though they were undergoing degeneration and as though there were basal cell changes present.

Generalized Localized Myxedema.

The patient is a white, married woman aged 25, who is employed as a grocery clerk and who came under observation on Oct. 31, 1939 because of an eruption.

She stated that the eruption followed immediately a three week confinement to bed, due to severe influenza, in February 1938. The initial process was said to

have appeared about the extensor surfaces of the elbows as asymptomatic small, elevated, yellowish pink lesions, which seemed to contain fluid but from which no fluid could be expressed. The condition remained stationary for some time; but in March 1939 it extended over the arms, and in July a cluster of such lesions appeared at the base of the nose, with similar lesions on the legs.

The patient's general health has always been good. Her weight has increased from 128 pounds (58 Kg.) in 1934 to approximately 200 pounds (91 Kg.) at the time of this examination. Early in 1938 her menses suddenly stopped, although they had previously been normal, except for considerable pain. Since that time she has had cramps at the time when a normal menstrual period was due, but there has been no flow. She has observed an increasing frigidity. There has been no drug ingestion except occasionally the chewing of gum containing phenolphthalein, and this seems to have no effect on the eruption.

There is no history of familial disease. The patient has been married seven years, and the husband is living and well. There have been two pregnancies, both of which resulted in unexplained miscarriage, the first occurring at the sixth month and the second at one and one-half months.

The patient presents an eruption which tends to be symmetric and whose primary lesion is a small, elevated, rounded, pink to waxy-colored, translucent papule. Certain of these have remained discrete, while others have coalesced to form plaques of varying size and shape. The eruption is observed at the glabella, on the left brow, on each side of the cheek, in both gluteal areas, on the extensor surfaces of the arms and forearms, on the anterior surface of each thigh immediately above the knee and on the posterior and lateral surfaces of the legs and ankles.

Urinalysis on several occasions gave negative results. There was 12 Gm. of hemoglobin per hundred cubic centimeters of blood. A blood count showed red cells 3,550,000 and white cells 11,400, with differential ratio of band cells 1 per cent, adult polymorphonuclear leukocytes 75 per cent, lymphocytes 20 per cent and large monocytes 4 per cent. The Wassermann and Kahn reactions and the reactions to Kline and Mazzinni tests were negative. A tuberculin test with a dilution of 1:10,000 elicited a negative reaction. A 1 per cent solution of congo red injected into a papule was not retained. The basal metabolic rate on one occasion was —2 per cent and on another occasion +1 per cent. A sugar tolerance test showed a fasting blood sugar value of 93 mg. per hundred cubic centimeters; the specimen taken one-half hour after administration of dextrose showed 178 mg. and one hour afterward 183 mg. Studies of the blood lipids showed: cholesterol 208 mg. per hundred cubic centimeters on one occasion and 158 mg. on another occasion, with cholesterol esters 156 mg. and lecithin 140 mg., the total lipids being 1,770 mg. per hundred cubic centimeters. Early reports on estrogenic studies indicated that there was little, if any, estrogenic substance present. Roentgenographic studies of the skull, humeri, femurs and chest showed no abnormalities except for some calcareous scarring in the base and hilus of the left lung. General physical examination showed no abnormalities.

Biopsy specimens were taken from several locations and studies by pathologists (Drs. Montgomery, Wedman and Culbertson), and each reported a diagnosis of localized myxedema.

In the period between Dec. 28, 1939 and Feb. 8, 1941 the patient had received at times thyroid, estrone (theelin) and whole anterior pituitary extract (polyansyn), without relief—in fact, with an accentuation of the old lesions and formation of new ones. She was seen by Dr. Paul O'Leary, who concurred in the diagnosis.

DISCUSSION

DR. LOUIS C. BRUNSTING, Rochester, Minn.: The diagnosis is well established on the basis of the histologic sections. The condition in this case is probably more extensive than in any case of this disease on record. The widespread disseminated discrete nodules suggest for a moment the appearance of systematized amyloidosis or ganglioneuroma, but on the arms and legs the lesions have coalesced to form the brawny plaques typical of circumscribed myxedema. In this patient's

case the usual history of operation for exophthalmic goiter is lacking. On the contrary, there was antecedent influenza and then a disturbance in the menstrual cycle with obesity. I have no suggestions regarding treatment. Thyroid seems to have been given a thorough trial.

DR. JOHN E. DALTON, Indianapolis: Two cases of this condition have been presented before the Cincinnati Society of Dermatology and Syphilology. Shortly after I presented this woman for the first time, Dr. Barrett showed an older man who exhibited essentially the same picture.

I have not seen this patient for three months, and at this time I am particularly interested in a new crop of papules which have developed on the extremities. Whereas previously the lesions had coalesced into plaque formations, these occur singly.

On reviewing the literature, I could find but 1 case of a condition which had a similar description (Neumann, H.: *Dermat. Wchnschr.* **101**:1263 [Oct. 12] 1935).

DR. CAREY C. BARRETT, Lexington, Ky.: The condition of the patient I presented looked exactly like that of this patient. He was a man aged 63. Biopsy specimens were studied by Drs. Weidman and Montgomery, both of whom agreed on a diagnosis of myxedema.

DR. RICHARD S. WEISS, St. Louis: What is the general experience with regard to the basal metabolic rate in this type of case?

DR. JOHN E. DALTON, Indianapolis: In the case Neumann reported the patient had a normal basal metabolic rate, as did this patient. Unfortunately, the patient of Dr. Barrett died before the rate could be determined.

DR. MARTIN F. ENGMAN JR., St. Louis: I should like to clear up in my own mind the question of whether localized myxedema is a thyroid deficiency reaction. I think that in this particular case there is some question as to the propriety of using the term myxedema. Myxedema implies a thyroid dysfunction. I should like to hear that stand defended.

DR. JOHN E. DALTON, Indianapolis: I agree with Dr. Engman that the diagnosis of generalized localized myxedema is a misleading term and propose the designation of mucoid papular disease or lichen myxedematosus, as used by Neumann for the condition in his case.

Blastomycosis.

L. B., a white woman aged 58, a schoolteacher, was first seen on Dec. 12, 1940 with an ulcer on the upper, inner part of the left thigh of three months' duration. It began as a red nodule that slowly enlarged. It was opened on several occasions by her family physician. The lesion slowly enlarged to 1½ inches (4 cm.) in diameter with a central ulceration and typical verrucous projections about the edge that exuded pus on pressure. Smears of this pus exhibited double-contoured budding yeast cells. One week before she was seen a nodule appeared on the proximal phalanx of her left index finger; this has never opened or caused any pain.

Roentgenograms of the chest, as well as the results of all the laboratory tests, were normal. Histologic examination showed a granulomatous infiltrate, as well as the double-contoured yeast cells, confirming the diagnosis.

The patient lived on a farm for a time during the past summer. She has had roentgen therapy and iodides by mouth since the first day she was seen, with considerable involution of the lesions.

Blastomycosis.

The patient, a white woman aged 48, was first seen on Jan. 6, 1941. She stated that two years previously her family physician had treated two granulomatous lesions, 1 cm. in diameter, on the right leg. Smears at that time showed blastomycetes. Cauterization with silver nitrate, oral administration of potassium iodide and local application of ammoniated mercury ointment produced involution. She had no further trouble until six to eight weeks ago.

At present there are five granulomatous lesions on the lower half of the legs clinically typical of blastomycosis. The largest one is half the size of the palm. The patient has mild diabetes, which is under control, heart disease of long standing, severe bursitis of both shoulders of long standing, a gallbladder which cannot be visualized and psychoneurosis.

The Wassermann and Kahn reactions of the blood were negative. The fasting blood sugar value was 127 mg. per hundred cubic centimeters. The hemoglobin amounted to 74 per cent (12.4 Gm. per hundred cubic centimeters), and a blood count showed red cells 4,900,000 and white cells 7,300, with a normal differential ratio. Roentgenograms of the chest and shoulder joints showed no abnormalities.

Histologic examination showed blastomycetes (acid-fast stain), as did also direct smear cultures (sodium hydroxide preparation).

The lesions are improving rapidly with the following therapy: 90 grains (6 Gm.) of potassium iodide daily by mouth, roentgen therapy (175 r) weekly to each lesion for five doses and 5 per cent potassium iodide ointment to the lesions twice daily preceded by scrubbing with soap and water.

Blastomycosis.

A white man aged 41 has had a small pimple on the nose since May 1938 from which blastomycetes were cultured. With the administration of roentgen therapy (1,900 r to the neck, 1,500 r to the cheek and 840 r to the left ear) and iodides and the application of 5 per cent cupric sulfate ointment the lesions improved for several months and then recurred after the use of ammoniated mercury ointment, phenol and silver nitrate. At present he has lesions on the mucous membrane in addition to those on the skin.

The Kahn reaction was negative, and the urine was normal. The hemoglobin amounted to 16 Gm. per hundred cubic centimeters, and a blood count showed 5,500,000 red cells and 15,000 white cells.

Histologic examination showed blastomycetes.

Blastomycosis.

A white woman aged 60 had her first lesion in September 1940. The lesions have spread gradually. To date she has had roentgen therapy (800 r) and iodoethenamine. The urine and a blood count were normal. A Kahn reaction was negative.

DISCUSSION OF CASES OF BLASTOMYCOSIS

DR. CAREY C. BARRETT, Lexington, Ky.: I should like to comment on the unusual opportunity of seeing so many examples of this condition in women. It is usually a disease of men.

DR. LAWRENCE C. GOLDBERG, Cincinnati: I have had the opportunity of seeing 5 patients with blastomycosis in the last year; 2 of these had blastomycosis of the lung, and both are living today.

DR. EARL W. NETHERTON, Cleveland: It is unusual to encounter a group of cases like this in this part of the country. At first I thought the condition in the second case was bromoderma, because of the honeycombed surface of the skin, with pitting as though plugs or comedos had been removed from the follicles. The patient complained that the lesions were painful and stated that she had been taking a nerve sedative for some time in the past.

DR. D. J. KINDEL, Cincinnati: Concerning the second case, the lesions have not been cultured, but in looking at the section there is no question about the finding of blastomycetes. Two years ago blastomycetes were found in direct smears. At the time the patient was first seen the evidence seemed conclusive and I did not culture material from the lesions, but the organisms were present in the section without any doubt. One cannot rely on this patient's complaints, for she has been an invalid for twenty years and has a variety of complaints, which are greatly exaggerated.

DR. NORMAN TOBIAS, St. Louis: How does Dr. Kindel account for the appearance of blastomycosis in this region? Cutaneous types usually occur on the face, neck or dorsa of the hands.

DR. D. J. KINDEL, Cincinnati: I do not know how to account for the pathogenesis. The majority of patients seen here have come from rural areas. Two male patients handled hogs.

DR. ELMORE B. TAUBER, Cincinnati: After the publication of Dr. Gilchrist's article and then Dr. Hyde's, a great number of cases, 20 to 25 in a year, were observed. Recently more and more cases have occurred. The patients have come from the great rural area around Cincinnati.

DR. H. J. PARKHURST, Toledo, Ohio: I should like to agree with Dr. Netherton in regard to the second case.

DR. A. H. CONRAD, St. Louis: The second patient stated that she had had some treatment for her neurologic complaints, and on superficial examination the condition had somewhat the appearance of bromoderma. After closer examination, however, I am of the opinion that the condition is blastomycosis. Recent treatment has undoubtedly changed the appearance of the lesions.

DR. ELMORE B. TAUBER, Cincinnati: I agree with the diagnosis of blastomycosis in the second case, but for years this patient has been taking nerve medicine containing bromide which would have some effect on the lesion. I think it could have exaggerated the eruption of blastomycosis.

DR. M. F. ENGMAN JR., St. Louis: I agree with Dr. Netherton. At a meeting in St. Louis 2 cases were presented, one of proved blastomycosis and the other of proved bromoderma. In each case the eruption was on the wrist. It was impossible to distinguish between the two conditions. This patient has had a considerable amount of potassium iodide. I wonder whether bromoderma would improve with potassium iodide treatment. I do not believe it would.

DR. I. J. ARNSSON, Buffalo: While bromoderma and blastomycosis may look alike clinically, one look at the histologic slide will tell the difference. The section from the second case rules out bromoderma. In bromoderma one would expect round cellular infiltration around the sudoriferous apparatus, which was absent in this particular case.

DR. CAREY C. BARRETT, Lexington, Ky.: With regard to the statement that blastomycosis is seen most commonly in patients from rural regions, it is interesting to note that there is no disease of livestock recognized as blastomycosis.

DR. KARL G. ZWICK, Cincinnati: As far as my experience goes, I find it impossible to differentiate by their appearance the cutaneous lesions of iododerma from those of bromoderma, and this patient has received ample doses of both iodides and bromides.

DR. RAYMOND G. SENOUR, Cincinnati: In answer to Dr. Engman, it seems to me that the administration of potassium iodide would make the lesions of bromoderma worse.

DR. EARL W. NETHERTON, Cleveland: I did not mean to leave the impression that I was making a definite diagnosis of bromoderma. I think material from the lesions ought to be cultured. I could not see the organisms in the section. There was a contrast between the section in this case and the sections in the other cases. As far as sweat glands are concerned, there was one area where one sweat gland was present. If other sections were made one might find other glands with an inflammatory infiltration about them. As far as iodides are concerned, I did not have the impression that iodides could influence the course of bromoderma. I believe that iodides usually produce a bullous or nodular eruption of a different type. The second patient presents a granulomatous lesion with a honeycombed appearance similar to that of bromoderma, in contrast to that produced by iodides.

DR. A. H. LANCASTER (by invitation), Knoxville, Tenn.: I do not question the diagnosis of blastomycosis, but it is true that the patient's condition has many of the characteristics of a bromide eruption. Some patients with blastomycosis when given iodides have an acute exacerbation of an inflammatory nature due to a sensi-

tivity to the dead organism. At times it is necessary to desensitize these patients with a vaccine, after which they tolerate the iodides and healing takes place in a satisfactory manner.

DR. NORMAN TOBIAS, St. Louis: I believe an intradermal test with blastomycin should be made in this case to corroborate the diagnosis. It seems that some doubt exists as to whether blastomycetes are present in the section. The blastomycin test is of value only as collateral evidence. By itself it is no more dependable than the luetin test in cases of late syphilis.

Sarcoma of Kaposi Beginning at Five Years of Age.

A white unmarried man aged 20, employed as a lathe operator, came under observation on Sept. 3, 1940 for an eruption involving the left foot, ankle and leg.

The history revealed that he entered the James Whitcomb Riley Hospital for Children, Indianapolis, on May 31, 1924, at the age of 5 years. There he presented swelling, tenderness and increased sweating of the dorsum of the left foot, prominence of the left trochanter, a tender tumor-like mass over the left sacroiliac joint, limitation of abduction and extension of the left hip joint and muscular atrophy of the left thigh and leg. He was undernourished and complained of an asthenia. All these findings were said to date from the time of delivery, which was said to have been somewhat difficult owing to a breech presentation. Carious teeth were extracted during his hospitalization. Tests of the urine, blood counts and serologic tests revealed no abnormality.

A roentgenogram of the entire pelvis on May 31, 1924 showed the symphysis rotated to the right. The left ilium was of irregular density, apparently because of decreased calcium content in the upper portion and increased calcium content in the lower portion. On March 7, 1925 a roentgenogram of the lumbar portion of the spine showed incomplete fusion of the posterior laminas of the fifth lumbar vertebra without defect; the posterior laminas of the sacral segments appeared to be poorly developed, giving the appearance of a spina bifida occulta. On Sept. 14, 1925 a roentgenogram showed a reticulation of the left pubis and to a lesser degree a similar finding in the left acetabulum and in the left lower part of the ilium and narrowing and poor development of the upper shaft of the left femur. A roentgenogram of the pelvis on Aug. 29, 1928 showed changes involving the lower portion of the left ilium and the left pubis, which were difficult to account for in the absence of an infection. Thus it was said that it seemed probable that there was a dystrophy of the bone involving the ilium and pubis, which suggested osteitis fibrosa. Considerable deformity of the left side of the pelvis had occurred with considerable sclerosis in the lower portion of the left ilium just above the acetabulum. The aforementioned reticulation in the left pubis was still present and somewhat greater in its extent. The spina bifida occulta was still present in the fifth lumbar and first and second sacral vertebrae.

At that time the left iliotibial band was severed and a plaster spica was applied to hold the left lower extremity in the correct position. This spica was kept in place for four to six months. A photograph definitely showed swelling of the left foot and discoloration of the skin of the dorsum of the left foot which extended upward to encircle the left ankle. Further, it was noted that there was "some peculiar mottling of the anterior surface of the left thigh."

In the intervening years the lesion of the left foot and ankle extended to involve the lower half of the leg, became deep purplish and was associated with tenderness and occasional itching. There also developed a distinct area of mottling on the anterior surface of the left thigh below the groin and a similar area on the left buttock.

On Sept. 3, 1940 the patient presented an indurated brownish purple plaque with somewhat irregular shape and surface covering the dorsum of the left foot and encircling the left ankle and lower half of the left leg. On the anterior surface of the left thigh in its upper third there was an elevated tumor, approximately 5 inches (13 cm.) in diameter, which was doughy on palpation. The overlying skin in this area showed a network of telangiectatic vessels with punctate macular

purplish points scattered through them. A similar process was present on the left buttock. Because it was thought that this condition was a muscle displacement due to the patient's deformity, orthopedic consultation was asked for, but the opinion was that the lesion was in both instances a definite subcutaneous tumor mass. In the right groin several lymphatic glands showed enlargement, and one had reached the size of a walnut. There was also some question of a palpable gland in the middle part of the abdomen to the left of the spinal column.

Biopsy sections were prepared both from the cutaneous lesion of the left ankle and from the enlarged gland of the right groin. Both showed histologic changes compatible with Kaposi's sarcoma.

Treatment has consisted of unfiltered roentgen rays applied to the cutaneous lesions and filtered roentgen rays applied to the glands of the right groin.

DISCUSSION

Dr. Lawrence C. Goldberg, Cincinnati: I think this case deserves discussion because it is most unusual to find a hemorrhagic sarcoma of Kaposi in a 5 year old child.

Dr. John E. Dalton, Indianapolis: According to the history from the mother, even in infancy the patient presented swelling and tenderness of the left foot. At the age of 5 years when he entered the hospital these lesions were noted, but no diagnosis was reached. On the anterior surface of the left thigh and on the left buttock one sees early lesions of Kaposi's sarcoma, as manifested by minute purplish puncta scattered among many telangiectases. At present the patient shows essentially the same changes in the left pubic bone, the left ilium and the humerus that he did at the age of 5 years. These were checked by a roentgenologist, who like myself has never seen osseous changes in hemorrhagic sarcoma but who expressed the opinion that there is an association between the cutaneous and the osseous picture. Lesions of the bones in Kaposi's sarcoma were described by Scholz as early as 1899.

A Case for Diagnosis (Acrosclerosis? Rheumatoid Arthritis?).

A white man aged 60 states that his right hand began to swell in 1938 and the left hand in March 1940. Swelling extends from the fingers to the wrist but not above the wrist. There is never any redness or local heat. There is only pain on motion. Approximately in March 1940 also, the patient began to complain of pains in the shoulders and occasional swelling of the knees. There has been a loss in weight of 30 or 40 pounds (14 to 18 Kg.) in the last nine months. In addition to the joint disturbances, the patient complains also of occasional periods of severe vertigo. He has noted no discoloration or tenderness of the finger tips or of the toes. The patient was admitted to the hospital in January 1940 for treatment of first and second degree burns of the left foot, left ankle and right ankle, which healed without any reaction. He has also attended the varicose vein clinic for the past few months, where injections of sodium ricinoleate were given and two ligations of the saphenous vein were done. There were no complications attendant on this. There is a history of a moderate degree of congenital deafness. He had gonorrhea at the age of 22, with no recurrence. He has also had hay fever. There is a family history of tuberculous contact in recent years. The patient has worked as a lithographer, and in 1932 to 1935 he had two episodes of so-called "ink poisoning" with swelling of the hands and feet. No further details can be obtained on this reaction at present. Until recently the patient chewed one pouch of tobacco a day.

The general physical examination showed essentially no abnormalities. There has been some change in the features with suggestive firmness of the cheeks. The edema of the hands, atrophy, pigmentation and limitation of motion have not changed appreciably during the period of observation. A cold pressor test showed 20 to 22 mg. increase in blood pressure. There has been some cyanosis of the fingers on exposure to cold for the past six months. There has been a black

hairy tongue, which has improved to a slight degree. The blood pressure was 126 systolic and 58 diastolic. The microscopic sections have been normal.

The red blood cell count has varied from 4,000,000 to 6,000,000 and the white blood cell count from 8,000 to 9,000. The hemoglobin amounted to 10.2 Gm. per hundred cubic centimeters. Differential counts have been normal, with the eosinophils varying from 2 to 3 per cent. On September 7 the serum protein content amounted to 7.3 Gm. per hundred cubic centimeters; on October 7 it was 6.6 Gm., with the albumin 2.9 Gm. and the serum globulin 3.7 Gm., giving an albumin-globulin ratio of 0.78 to 1. On November 4 the serum protein amounted to 5.9 Gm. per hundred cubic centimeters, with 2.5 Gm. of globulin, giving an albumin-globulin ratio of 1.36 to 1. The basal metabolic rate on the same day varied from —6 to +3 per cent. Examination of the blood showed: calcium 11.6 mg. per hundred cubic centimeters, phosphate 4.5 mg., chlorides 5.6 Gm., cholesterol 2.04 Gm. and serum sodium 370 mg. (normal 325 to 350 mg.). A sugar tolerance test showed the following results: fasting, 78 mg. per hundred cubic centimeters; one-half hour, 126 mg.; one hour, 142 mg.; two hours, 144 mg., and three hours, 127 mg. An electrocardiogram showed increased voltage in the QRS complex. Venous pressure in the right arm was 3 cm. of water. Oscillometric readings were normal for the arms and legs. Fluoroscopic examination of the chest showed no abnormalities, but roentgenographic studies showed bilateral apical pulmonary tuberculosis (inactive?); there were no supernumerary ribs. Further roentgenographic studies showed general atrophy of the bones of the hand and narrowing of the articular spaces of the shoulders and knees, with little evidence of hypertrophic arthritis in the extremities but some in the bodies of the lumbar vertebrae. There was no calcification of the adrenal glands. There were bony lipping of the pelvis and an increase in osseous density around the sacroiliac joints, and several cystic areas were seen around the hip joints. A culture of material from the tongue showed Monilia albicans. A histamine wheal on the dorsum of the right hand gave maximum response in eleven minutes.

Histologic examination showed moderate acanthosis, some increase in pigmentation (in the basal cell layer) and edema of the cutis, with separation and splitting of collagenous fibers. The blood vessels were fairly numerous and showed no change.

Therapy has consisted of the administration of nicotinic acid and riboflavin, infra-red irradiation, diathermy and massage to the hands. The taking of brewers' yeast had no effect on the tongue. There has been no change in the patient's condition during an observation period of six months.

Scleroderma with Vaginal Lesions.

The patient, a white woman aged 55, states that she has had a white vaginal discharge since puberty accompanied by itching and painful burning. There have been tender lesions in the vagina and on the external genitalia since 1934. In April 1936 itching, burning, reddened areas developed on the flexor aspects of both forearms. No further lesions appeared until the spring of 1940, when other areas became involved. There has been a tendency toward symmetric distribution with involvement of the shoulders over the clavicles, the axillas, the elbows, the presternal region, the lower part of the abdomen, the intergluteal region from over the sacrum to the coccyx and the popliteal spaces. The lesions showed a gradual transition, the skin becoming thickened, hard, white and either smooth or roughened. At one time there was some impairment of motion at the shoulder joints due to involvement of the axillas and also a sense of "pulling" of the skin of the lower part of the abdomen when the arms were raised.

There are patches of white, smooth, moderately infiltrated skin over the clavicles and in the supraclavicular areas, axillas, presternal region and popliteal areas. The skin of the lower part of the abdomen is diffusely involved with atrophic scarring and hyperpigmentation. Over the lower part of the sacrum and coccyx is a well demarcated light brown, slightly scaly, infiltrated patch of skin. The lesions are bilateral and symmetric or in a midline distribution.

The vaginal mucosa and vulva present numerous small white atrophic lesions.

The remainder of the physical examination showed no abnormalities except for a bradycardia (pulse rate, 56 to 60). There are no signs of hypothyroidism.

The basal metabolic rates are said by the patient to have been consistently on the "minus" side, but within normal limits.

The hemoglobin amounted to 14.8 Gm. per hundred cubic centimeters of blood. A blood count showed 4,470,000 red cells and 5,400 white cells, with a differential ratio of 62 per cent polymorphonuclear leukocytes, 33 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. The urine was normal. The Kahn reaction was negative. The calcium concentration in the blood was 10.8 mg. per hundred cubic centimeters.

Histologic examination of material from the lesion in the lower part of the sternal region showed thin epidermis with vacuolation of the basal cells, few blood vessels and parallel huge collagenous fiber bundles.

Therapy has included thyroid medication, ultraviolet and roentgen irradiation and massage. The lesions have become softer and have diminished considerably in extent.

Linear Scleroderma.

U. A., a white woman aged 32, first noted a brown patch on the flexor surface of the right forearm one year ago. It was surrounded by an area of erythema and was tender. She noted loss of power in her right hand as the eruption spread in linear fashion up and down the arm. From erythema it faded to the typical irregular atrophic patches, with loss of pain and edema. In a year's time it has spread to the arm and shoulder, with resulting difficulty in abducting her arm. A violaceous halo and some telangiectasia are seen. Strength is returning in the arm. One month ago the back of the left hand became swollen and tender, with atrophy appearing on the arm.

Her original lesions appeared a few months after the birth of her last child, who is now 17 months old. Her general health has been good except for pyorrhea and many carious teeth. She has four children, living and well. Her Kahn reaction has been negative several times. The blood calcium was 9.9 mg. per hundred cubic centimeters and the blood phosphorus 2.6 mg., the ratio being about 4 to 1—a little low.

Her only treatment has been the application of a bland cream and the oral administration of salicylates.

A Case for Diagnosis (Lichen Sclerosus et Atrophicus?).

The patient, a white man aged 28, a furrier, has always enjoyed good health with the exception of having the present eruption. He had two small cutaneous tumors removed from the wall of his chest when he was an infant. He was born in Vienna, Austria. During the war, when he was 4 years old, he moved to Hungary and lived on a farm for three years. He thinks that his eruption appeared then. He had no subjective symptoms and was never examined by a physician until he was 9 years of age, when he was examined and passed by the American immigration authorities at Hamburg, Germany. As far as he knows, the eruption has not spread since he came to America except for one small linear area on the left arm which appeared two years ago following a trivial cut in the skin.

The patient is a well developed man with no abnormalities except the eruption, which is confined to the upper half of the trunk and to the arms. The lesions consist of large, irregular, atrophic patches symmetrically distributed on the shoulders and arms, between the thumbs and index fingers, around the right nipple and on the lateral wall of the chest on the right side. The central parts of the larger patches are approximately of normal color, and the superficial blood vessels are easily seen through the skin. On the margins of most of the larger patches there is a white, slightly scaly border, 1 or 2 cm. in width. There are many small discrete patches on the shoulders, which seem to be centered about follicular openings, as in atrophic lichen planus. These areas are 2 to 4 mm. in diameter and are chalky white.

The Wassermann and Kahn reactions were negative. Routine examination of the blood showed no abnormalities.

DISCUSSION OF CASES OF SCLERODERMA

Dr. John B. Squires, Cincinnati: In the first case, I believe the condition is hyperparathyroidism. Roentgenograms of the pelvic bones show osteoporotic changes, and this, along with the atrophy in the bones of the hands, would definitely suggest hyperparathyroid disease in spite of the fact that the concentration of calcium in the blood is not high and that the other changes in the blood are not remarkable. I believe the only other entity to be considered is osteoporosis on the basis of trauma. After a rather trivial trauma, such as a sprain or a Colles fracture, many persons have persistent swelling of the affected hand or extremity and osteoporosis.

In the third case the osseous changes are those of an actual osteoporosis. I do not think this man has an actual cutaneous disease.

Dr. Elmore B. Tauber, Cincinnati: Dr. Herman presented the first case at the vascular disease clinic; a diagnosis was not made.

Dr. Joseph Grindon Jr., St. Louis: The condition suggested by the linear distribution in these cases appears to be similar to that which I recently saw in a man with clinical morphea. This patient had a sclerodermatous patch on the right side of the abdomen for one year. Recently a similar patch appeared in an exactly symmetric position on the opposite side. In addition, this man has typical Raynaud's disease of the fingers. The exactly symmetric distribution of the morphea plus the presence of Raynaud's disease in my case and the linear distribution in the cases presented would seem to indicate that this condition is directly associated with some nervous disorder. It suggests that localized scleroderma and morphea may be dependent on trophoneurosis.

Dr. Louis A. Brunsting, Rochester, Minn.: It is my impression that the condition of the 55 year old woman who was presented as having scleroderma with vaginal lesions should be classified instead as lichen sclerosus et atrophicus on the basis of the character and distribution of the lesions, which include the vulva. There is a resemblance to scleroderma as well as to atrophic lichen planus, and the involvement of the genitalia by itself might be taken for kraurosis vulvae.

I believe, too, that the fourth patient, presented for diagnosis, shows unmistakable features of lichen sclerosus et atrophicus, and the microscopic picture is confirmatory.

Dr. Roy L. Kile, Cincinnati: I have followed the third patient for about a year. Shortly after the development of the eruption she lost power in her right hand. Since I first saw her she has regained this. In the last two months atrophy has been developing in the left forearm, and its evolution is following the same course as in her right arm.

Dr. John B. Squires, Cincinnati: In the third case I wonder if mecholyl (acetylbetamethylcholine) has been considered.

Dr. Roy L. Kile, Cincinnati: I have thought of using mecholyl iontophoresis, and I have used it in several cases. I do not know how valuable it is, and there would be some technical difficulties in its application in this case.

Dr. Arthur E. Schiller, Detroit: I have used mecholyl and iontophoresis in this type of case with rather indefinite results. In a patient with a considerable amount of disability I recently administered dihydrotachysterol, and the results have been rather encouraging. I do not believe I have used it long enough or in enough cases to know what the end results are. I checked on the calcium content of the blood at the same time.

Dr. Harold R. Vogel, Pittsburgh: I think that the condition in the first case fulfils the requisites for a diagnosis of acrosclerosis. This is a systemic disease, not confined to the skin, and changes in the bones are found in all proved cases. The history of onset and progression is typical. I had the opportunity of studying

a case thoroughly for a time; calcium determinations were always within normal limits; mecholylchloride (acetylbetamethylcholine hydrochloride) was tried, and ulcerations developed. This drug, if used in cases of this type, should be tried cautiously.

DR. ELMORE B. TAUBER, Cincinnati: When this patient recently came into the hospital there was a definite line of demarcation with a great deal of pigmentation; there was also a condition of the tongue like that in pellagra. I made a diagnosis of pellagra. With the peculiar changes there was a suggestion of two distinct conditions. That was why brewers' yeast and nicotinic acid were administered. The tongue is clear now and the hands are somewhat improved, but the peculiar sclerosis remains.

DR. CAREY C. BARRETT, Lexington, Ky.: I thought the condition in the last case was lichen sclerosus et atrophicus, but I thought it was extraordinary because of the wide distribution.

Lupus Erythematosus; Vasomotor Instability.

The patient, a barber aged 33, was first seen on Jan. 10, 1935. He has had the eruption five and one-half years. He was seen seven times in January and February and then moved to Cleveland. For the past year or more he has been seen regularly at the Cleveland Clinic.[1]

1. The information regarding this patient was supplied by Dr. Earl W. Netherton.

The skin is florid, with numerous telangiectases. An erythematopapular eruption appears suddenly on the neck, face, arms and chest and may last three or four days to two to three weeks, when it disappears. This has occurred on many occasions. The papules seem to be infiltrated and are never associated with itching on the face but at times itch on the arms and chest. He has taken headache powders which contain acetanilid, potassium bromide and acetylsalicylic acid, paraldehyde by mouth and bromides, but none for several months. He is of a hypochondriac type and is convinced that the eruption changes with the moon. A patch test with quinine gave negative results.

The ascorbic acid content of the blood was 0.85 mg. per hundred cubic centimeters, which is low. Repeated studies of the blood and analyses of the gastric contents after Ewald test meals gave no information. The basal metabolic rate was —2 per cent. Studies showed no blood dyscrasia. Vasomotor tests (hands in water at 10 C. for ten minutes), examination of the stools and a Kahn test of the blood gave negative results.

At the Cleveland Clinic the patient was given 300 mg. of ascorbic acid daily, with no improvement. A bismuth preparation taken internally and local applications likewise caused no improvement. Roentgen therapy was tried. The side irradiated showed improvement in one week, in contrast to the control side of the face. The evanescent appearance and the disappearance of the eruption without treatment are striking.

DISCUSSION

DR. B. F. BARNEY, Columbus, Ohio: I have a personal interest in this case. For the past fifteen years I have been afflicted with the same condition. It might be of interest to cite my recent experience.

I was relatively free in Ohio and then went to the Gulf coast, where seafood was abundant. I partook freely of it and had an exacerbation. On returning home the condition cleared up and did not recur until I ingested a large quantity of chocolate. Two days later it flared up with definite urticarial papules that sometimes became confluent and resembled lupus erythematosus. When the papules started to clear they scaled, resembling scaling lupus erythematosus. There was no blocking of the follicles, telangiectasia or scaling, however, when the process was active. I think it would be well to investigate this patient along a similar line with a common sensitizing agent.

DR. EARL W. NETHERTON, Cleveland: Dr. Curtis and I followed this patient for some time. We studied his condition a great deal except, as Dr. Barney mentioned, from the standpoint of allergy. At one time he looked as though he had lupus erythematosus. That is why we gave him a bismuth preparation. I believe, as Dr. Lane suggested, that the eruption probably belongs in the erythema group, but we could not find its cause. At first we thought it was a drug eruption, but we can now say positively that it was not. When he goes out in the sun he has an attack.

DR. RUTH HERRICK, Grand Rapids, Mich.: I should like to know whether the patient has been tested with perfume. He is a barber, and many hair lotions contain perfume.

DR. B. F. BARNEY, Columbus, Ohio: In going back in my history, Dr. Keim made the diagnosis when the eruption was in papular form, and I was given small doses of a gold compound, to which the condition responded.

With regard to photosensitivity, which Dr. Netherton mentioned, I think if the patient continues to have the eruption the photosensitivity will disappear. There was a time when I could not go into the sunlight, but subsequently the eruption was benefited by ultraviolet radiation and roentgen rays. I have had all the patch tests and all the allergy tests, with negative results. I have gone into the history of drugs, and there are no drugs which seem to influence the occurrence of attacks. There are many cases in which a condition of this kind comes on within a few hours or within a day, but that has not been true with me. In going back over my history, up until fifteen years ago I ate very little seafood. I think it will be found that this man may have a similar sensitivity.

DR. D. J. KINDEL, Cincinnati: I saw this patient first in 1934, and then he moved to Cleveland and stayed there four or five years. There is one point on which I am inclined to agree with the patient: The phases of the moon may have something to do with the attacks. He has been given patch tests with the common things he uses, particularly quinine. I may have to admit the diagnosis of lupus erythematosus under pressure. He came back last night after two weeks' sojourn in North or South Carolina. He had no eruption when he left here. He has been presented a number of times before the Cincinnati Dermatological Society, sometimes with a flare-up and sometimes without. Recently I checked his basal metabolic rate. I had him immerse his hands in water at a temperature of 10 C. and was unable to get the same response that Dr. Netherton got some time ago. The last time I saw him, and the only time, I gave him ultraviolet irradiation.

DR. RICHARD S. WEISS, St. Louis: It is possible that both of the contending groups that have discussed this case are right. There undoubtedly is vasomotor instability. With it the patient presents lesions that are definitely of the erythema type, and his various eruptive phenomena are apparently produced or at least made worse by sunlight. Some of the lesions on his face are small slightly scaly plaques which are definitely not evanescent. The lesions on the trunk are urticarial and erythematous. I think that the condition is chronic disseminated lupus erythematosus. It is well known that this condition will from time to time show urticarial and erythema-multiforme-like lesions which are evanescent.

DR. ADOLPH LOVEMAN, Louisville, Ky.: Dr. Barney has lived in Cleveland, Ann Arbor, Mich., and Columbus, Ohio; so he has lived, obviously, in the "goiter belt." I suggest that he stop taking iodized salt, since he has flare-ups following the ingestion of seafood.

DR. B. F. BARNEY, Columbus, Ohio: I have never taken iodides internally, and for several years I have not taken iodized salt.

DR. LAWRENCE GOLDBERG, Cincinnati: I believe that when a patient presents a definite histologic picture of lupus erythematosus but a clinical picture of a disease of the erythema group, the histologic diagnosis should prevail.

DR. I. J. ARNSSON, Buffalo: The histologic picture in this patient does not suggest anything typical for lupus erythematosus, but rather it supports the suggestion of Dr. Lane. Two characteristic features are seen in the slide: one is the

dense infiltration around the deep blood vessels in the cutis, and the other is the edema of the subpapillary layer. There is no infiltration in the subpapillary layer. This picture does not go with lupus erythematosus.

Late Syphilis with Juxta-Articular Nodes.

For the past twenty-five years this patient, a white woman aged 65, has had recurrent crops of cutaneous lesions on the extremities. The first lesions appeared on the fingers. They have appeared in the summer; they itch slightly at the start and disappear during the winter. Ten years ago the patient had painless hard swellings on the forearms just below the elbows. At present she also has diabetes and varicose veins, both of which are being treated.

The initial examination of the patient revealed the following changes: Above and below the elbows were glossy, pink, smooth, firm, slightly elevated nodules arranged in circinate and polycyclic patterns. Similar lesions were present above both knees, on the right knee and on the dorsal aspect of each wrist. Below each olecranon process were nodules varying in size from that of a pea to that of a walnut. The skin was normal over them. They were not tender.

Examination at present reveals an elevated round firm subcutaneous nodule below the left elbow. A few irregular reddish patches are noted on the forearms.

The Kahn reaction was 3 plus. The urine was normal. A blood count showed 4,500,000 red cells and 7,000 white cells, and there was 12.4 Gm. of hemoglobin per hundred cubic centimeters. Histologic examination showed dense interlacing fibrous tissue masses of perivascular infiltrate with some degree of endarteritis. No thrombosis or necrosis was noted.

The patient has been given twenty weekly injections of a bismuth preparation (40 cc.). Several of the subcutaneous nodules have disappeared; only a few of the original infiltrated configurate lesions are present, and these have lost their induration.

Late Syphilis with Orbital Gumma.

A Negress aged 60 in November 1939 began to have left frontal headaches and pain in the scalp above the left eye. These continued until May 1940, when her left eye became painful and swollen. The vision was greatly reduced and her left eye would not "move." Gradually the pain and swelling subsided. During the latter part of October 1940 she had a recurrence of these symptoms. The left eye became closed. When held open, double vision was noted. During the original episode the patient had a "blood test" done by a private doctor. It showed "bad blood." She then received four or five weekly injections in the arm. No history of primary or secondary lesions of syphilis was elicited. There have been no miscarriages.

In November 1940 examination of the left eye showed exophthalmos and paralysis of the levator palpebrae and the other extensor ocular muscles. The pupil was dilated and fixed. There was partial loss of sensation to light touch over the upper eyelid. Visual fields were constricted. There was extensive destruction of the nasal septum. The left inferior and middle turbinates were absent. Saddle nose was present.

The Kahn reaction was 3 plus. The reaction to a Wassermann test of the spinal fluid was positive. Spinal fluid protein was 94 mg. per hundred cubic centimeters. The Pandy test showed negative results. A blood count showed 5,270,000 red cells and 9,000 white cells, and the hemoglobin amounted to 16.4 Gm. The urine was normal. A roentgenogram of the skull showed no involvement of the left orbit.

To date the patient has received five injections (2 cc. each) of a bismuth compound, one injection (0.6 Gm.) of neoarsphenamine and 10 drops of potassium iodide, three times a day. Her condition is much improved; there are less exophthalmos and less ptosis.

DISCUSSION OF TWO CASES OF LATE SYPHILIS

DR. LOREN W. SHAFFER, Detroit: In the first case I accept the diagnosis of late syphilis with juxta-articular nodes. It is rather surprising, however, to see the excellent clinical result that is being secured in this case, though I realize that the lesions will undergo involution under treatment.

The second patient has shown striking clinical improvement after a therapeutic test which substantiated the diagnosis.

Juvenile Xanthoma.

Several weeks after birth this 11 month old white boy had a few papular lesions on his abdomen and back. These persisted, and numerous other similar lesions have since appeared. Some of the earlier nodules have disappeared, leaving red or brown pigmented scars. New lesions have appeared from time to time. The general health is good, but there are some severe visual disturbances. The child is almost blind but retains light perception plus some degree of vision.

The birth history is normal. The family history reveals no evidence of cutaneous disease, diabetes or lipoid disturbances.

The child is well developed and well nourished. The skin presents numerous yellow, red and orange nodules of varying size and shape, most numerous on the scalp, face, neck, eyelids and upper portion of the trunk. Numerous dark red to brown areas, the sites of former tumors, are present. The lesions are nontender, freely movable and attached to the overlying skin. Fine capillaries and small blood vessels are seen beneath the surface of many of the tumors, and some show central indentation. New lesions cannot be induced by pinching or by other forms of trauma.

The general physical examination showed no abnormalities except for the condition of the eyes. The liver and the spleen were not enlarged. The ocular condition has been interpreted as buphthalmos (Dr. F. X. Siegel).

Roentgenograms of the skull and of the long bones were normal. Kahn tests of the mother and of the child gave negative results. The urine was normal. The following blood studies were performed by Dr. E. A. Wagner:

	6/10/40	6/20/40	8/5/40
Red blood cells	5,300,000	5,250,000	6,300,000
White blood cells	43,000	10,600	7,100
Hemoglobin	14.2 Gm.	17 Gm.	16 Gm.
Differential count			
Polymorphonuclear leukocytes	5 per cent	18 per cent	44 per cent
Lymphocytes	90 per cent	81 per cent	64 per cent
Monocytes	5 per cent	.....	.....
Eosinophils	.....	1 per cent	2 per cent

DISCUSSION

DR. NORMAN TOBIAS, St. Louis: I was under the impression that the condition in this case was Hand-Schüller-Christian disease because of the symptoms, ocular changes, cutaneous tumors and general appearance of the child. The syndrome is so protean in its manifestations that one never encounters 2 cases alike.

Histologic examination showed a thin epidermis. Below this a diffuse nonencapsulated infiltrate extended into the subcutaneous tissue. The infiltrate consisted of sheetlike masses of fibroblasts with extensive vacuolation of the cells (upper portions) and sheetlike masses of large cells with foamy cytoplasm and large vesicular nuclei in the lower portions. There were spotty areas of lymphocytic infiltrate at the edges of the section. Touton giant cells were scattered throughout. The scarlet red stain showed bits of extracellular and intracellular fat-staining material in various parts.

Some of the lesions have been treated by the application of solid carbon dioxide. The patient has been observed for about three months. During this time some of the lesions have disappeared spontaneously and some in response to the application of solid carbon dioxide. A few new lesions have appeared.

DISCUSSION

DR. LOUIS C. BRUNSTING, Rochester, Minn.: Xanthomatosis of this extent in a child is a rather serious disease. The ocular signs are those of an unusual form of glaucoma, I am told, but there appears to be some hydrocephalus and it may be that the Hand-Schüller-Christian syndrome is developing. Values for blood cholesterol are normal; the other lipoid elements should be determined. Moreover, the child should be checked from time to time from the standpoint of diabetes insipidus.

DR. ALFRED L. WEINER, Cincinnati: I should like to add some weight to the diagnosis under which the case is presented. I think Dr. Brunsting infers that this child's condition may be an early phase of Hand-Schüller-Christian disease. I shall try to study the child with that in mind.

The cholesterol content of the blood is 183 mg. per hundred cubic centimeters, which would favor the diagnosis of juvenile xanthoma, because in that condition the cholesterol is not elevated. The normal roentgenograms of the bones also are in favor of this diagnosis, though the roentgenologist noted some slight abnormality of the sella, but he was not willing to call it pathologic.

Regarding the eyes, the term buphthalmos, as I understand it, defines a type of glaucoma which is congenital in origin and has a bad prognosis. Sometimes surgical measures help, but as a rule children with the condition become blind. Buphthalmos should be differentiated from exophthalmos because the mechanism of production differs and because failure to do so adds to the confusion in the differential diagnosis of Hand-Schüller-Christian disease and juvenile xanthoma. Ophthalmoscopic studies of the fundi have not been made because, in view of the age of the child, a general anesthetic would be required. I do not think that any one could say that Hand-Schüller-Christian disease is not going to supervene here, but at present I think that there is little or no evidence of this condition.

Pyoderma Gangraenosum; Ulcerative Colitis (Healed).

G. R., a white man aged 31, a steel worker, has been ill since 1932. His illness began with the onset of intractable diarrhea accompanied by a long series of indolent, recurrent cutaneous ulcers. There was some correlation between the number and virulence of the cutaneous lesions and the severity of the diarrhea, but this had not been striking. The typical evolution of an ulcer was as follows: It began as a small vesicle or pustule, which rapidly broke down, leaving a deep necrotic area. Surrounding this was a purple-blue halo, beyond which was a rapidly advancing erythematous border. There was deep undermining; sloughing was rapid and extensive, leaving a dirty gray cribriform base. There was no malodor. Healing occurred in from six days to six weeks, depending on the size, site and extent, with resultant, atrophic, pigmented scars of serpiginous outline. The ulcers varied in size, shape, number and location, but any part of the body could apparently be affected. Trauma seemed to predispose to the development of ulceration; on several occasions typical lesions appeared at the sites of therapeutic inoculation. Exacerbations for the most part were insidious in onset and usually were unaccompanied with constitutional reaction or flare-up in the activity of the colitis.

The past and family histories were irrelevant. There was no history of syphilis or of tuberculosis. The patient had been hospitalized in various places and for varying periods.

Repeated physical examinations showed no abnormalities except ulcerative colitis. Repeated attempts (including examination on a warm stage) to demonstrate Endamoeba histolytica in the lesions of the colon and of the skin failed. Examination for blastomycetes and other fungi gave negative results. Hemolytic streptococci were the predominant organisms in the ulcerations of the skin and of the bowel. There was marked hypochromic anemia. All other laboratory tests gave negative results.

In April 1938 the patient was readmitted to the Cincinnati General Hospital from the Hamilton County Home and chronic Disease Hospital. At this time several typical large ulcers were present on the back, on the right hip and on the legs. The patient had been having eight to ten liquid bloody stools daily. Proctoscopic examination disclosed a picture typical of chronic ulcerative colitis, and hemolytic streptococci, staphylococci and colon bacilli were isolated. Except for anemia, debilitation and loss of weight, the general physical examination again showed no abnormalities.

The stools failed to reveal ova or parasites but showed gross and occult blood. Cultures of the stools showed hemolytic streptococci, staphylococci and colon bacilli. Cultures of tissue from cutaneous lesions showed hemolytic and nonhemolytic streptococci and colon bacilli but no amebas or fungi. The urine was normal, and the Kahn reaction was negative. The blood count showed 3,100,000 red cells and 8,800 white cells with a normal differential ratio. There was 8 Gm. of hemoglobin.

Histologic examination showed extensive areas of necrosis beneath an acanthotic epidermis. There were no giant cells or other characteristic changes and no amebas or fungi. Arterioles of the subcutis showed marked intimal proliferation.

The patient has had a variety of treatments, including transfusion, serums, vaccines, acetarsone, calcium and many types of local therapy.

Sulfanilamide was administered on the patient's fourteenth day in the hospital, and approximately 6 to 8 Gm. was given daily until a concentration in the blood of 11 mg. per hundred cubic centimeters was attained. General supportive measures were instituted, and the patient was given an occasional blood transfusion. At various times reactions to sulfanilamide occurred, including fever, cyanosis and purpuric eruptions, and on such occasions it was necessary to discontinue administration of the drug temporarily. It was always possible to resume the giving of sulfanilamide, however, so that a fairly effective concentration of the drug in the blood was maintained over a period of several months. During this time the healing of the colitis and of the cutaneous ulcerations was gradual rather than dramatic, and no new lesions appeared as long as the patient received sulfanilamide. It was thought to be significant that on several occasions when the use of the drug was stopped new lesions developed. Over a period of three months the disease was slowly brought under control. The skin was entirely healed; the colitis subsided, and the red blood cell count and the hemoglobin content were restored to normal. The patient was able to walk for the first time in more than eighteen months. He gained weight rapidly and was discharged on Nov. 26, 1938, after two hundred and thirteen days of hospitalization. At this time proctoscopic examination showed a great deal of healing in the large bowel, although rare hemolytic streptococci were still present in the stool.

The patient remained in good health and was free of diarrhea and cutaneous lesions for several months, until he suffered a minor bruise on his right thigh; on the site of the trauma a typical serpiginous ulcer developed. There was no recurrence of the colitis or anemia. The patient was readmitted to the hospital, and sulfanilamide (4 Gm. daily) was again administered until a concentration of 12 mg. per hundred cubic centimeters of blood was reached. The ulcer healed within two weeks, and the patient was discharged on Feb. 15, 1939. Since that time he has been carefully observed in the dispensary and given occasional small amounts of sulfanilamide. The patient was reexamined last in February 1940, and at this time there had been no recurrence of any of the symptoms. Proctoscopic examination showed much scarring but no ulcerations in the large bowel. Since that time the patient was not seen until the day of presentation.

DISCUSSION

DR. ALFRED L. WEINER, Cincinnati: The effect of sulfanilamide treatment in this particular case was dramatic. I should like to ask Dr. Brunsting if any of the patients in the original series have been brought back and treated with sulfanilamide or related drugs.

DR. F. M. JACOB, Pittsburgh: The response to sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in some cases of this kind is dramatic. I had such a case in Pittsburgh a short time ago. The eruption began with a small follicular pustule on the finger, to which the patient said he applied warm boric acid. The reaction was like a burn, and within twenty-four hours gangrenous areas developed on the opposing sides of two fingers. Sulfathiazole given in moderate doses for three or four days caused these gangrenous areas to separate, and they cleared up readily. In a week or ten days another pustule developed; with sulfathiazole therapy this lesion lasted only about two days.

DR. LOUIS C. BRUNSTING, Rochester, Minn.: The excellent results obtained here are to be commended. My associates and I have been encouraged in similar cases by a favorable response, although not invariably. It is necessary first of all to build up the general resistance by fortified diets, blood transfusions and the like and to anticipate untoward reactions in sensitive patients. It is a mystery why in certain patients with colitis a supersensitive skin will develop, metabolic abscesses will appear and not infrequently, at the sites of trauma, such as hypodermic injections, sterile abscesses will form. Sulfanilamide and its compounds are a valuable contribution to the treatment of this chronic, recurrent disease.

DR. HARRY M. ROBINSON (by invitation), Baltimore: I wonder if sulfanilamide is used locally by any one here. I have observed about 60 cases, including cases of eczema secondarily infected, in which sulfathiazole applied locally either in ointment form or in a greaseless base has proved much more effective than ammoniated mercury ointment or gentian violet.

DR. BENJAMIN LEVINE, Cleveland: I have used 1 per cent sulfanilamide dissolved in acetone and ethyl chloride on infected cutaneous lesions. I have treated about 18 patients with impetigo, and in 4 or 5 of them the condition cleared up in forty-eight hours, the rest in not over one week.

DR. ELMORE B. TAUBER, Cincinnati: I have been using sulfanilamide in both liquid and ointment form for epithelization and restoration of capillary permeability in burns. So far it has been rather remarkable.

DR. KARL G. ZWICK, Cincinnati: Sulfanilamide is only very slightly soluble in water or serum, and it can be used dry.

DR. ELMORE B. TAUBER: One can definitely get a concentration of the drug in the blood by local application, so it must be absorbed.

DR. G. VAN RHEE, Detroit: I have used either sulfathiazole or sulfanilamide locally with good results. Both drugs cause slight burning. The lesion usually clears in about forty-eight hours.

Favus.

This woman was seen for the first time the day before yesterday. The diagnosis is obvious from the clinical appearance of the patient and from examination of the hairs. There has not been time to make cultures.

DISCUSSION

DR. CAREY C. BARRETT, Lexington, Ky.: I occasionally see patients with favus coming from the mountainous areas of Kentucky. This is the fourth one I have seen from rural Kentucky, and they were nearly isolated from the rest of the world. Every one of the 4 lived at least forty miles away from the others and away from the mining centers in that territory.

DR. ELMORE B. TAUBER, Cincinnati: I had 1 case in Cincinnati, 2 from Tennessee and 3 from Kentucky.

DR. CAREY C. BARRETT, Lexington, Ky.: The patient told me she knows where she got the disease. A visitor at her home seven or eight years ago had the same thing. I am going to investigate the case from that angle, because I think I can locate that woman and examine her.

BRONX DERMATOLOGICAL SOCIETY

LEO SPIEGEL, M.D., *President*

HENRY SILVER, M.D., *Secretary*

Jan. 23, 1941

A Case for Diagnosis (Lupus Erythematosus Disseminatus? Senear-Usher Syndrome?). Presented by DR. GIRSCH D. ASTRACHAN.

V. M., a man aged 37, born in Italy, has been treated for psoriasis since 1938. He was admitted to the Metropolitan Hospital on Sept. 3, 1940. Two months previously there developed an exfoliative dermatitis, for which he did not seek medical aid until he became weak. He had had malaria in 1922.

On admission the patient presented a generalized eruption composed of many eroded areas which varied in size and shape; some of these were covered with thin crusts. Intact bullae and remains of broken bullae were seen. An intense odor was present. No lesions were noted in the mouth. There was conjunctivitis with a purulent discharge. On the nose and cheeks there was a scaly eruption of butterfly distribution. The borders of the lesions on the face were well defined.

The course of the disease was stormy for the first six weeks because of a septic type of fever, with daily rises in temperature to 103 and 105 F. Consultations with members of the medical, eye, ear, nose and throat departments failed to offer a clew to the cause of the fever. Roentgenograms of the chest, chemical examinations of the blood and repeated blood counts disclosed no abnormalities. The following treatment was given at the hospital: oral administration of calcium gluconate in large doses; vitamins B and C; liver extract, 0.25 to 2 cc. every other day; repeated blood transfusions; quinine sulfate, 10 to 15 grains (0.65 to 1 Gm.) per day for three five day periods; high colonic irrigations, and baths with potassium permanganate. The patient was discharged on December 14.

At present the eruption involves the scalp, face, trunk and upper extremities and is composed of scattered lesions which vary in size. Some of these are infiltrated and covered with scales or crusts. There are ruptured bullae with a serous discharge and many eroded and crusted lesions. On the trunk and on the lower extremities atrophic and depigmented spots are seen. There are crusted plaques the size of a palm, formed by coalescing lesions. On the face are seen several well defined and infiltrated scaly areas. In the sacral region there are several elevated lesions covered with thick silvery scales.

Urinalysis gave essentially negative results. The Wassermann reaction was negative. The examination of the blood showed secondary anemia with mild leukocytosis. The blood smears showed no organisms seen in septicemia or malaria. Histologic examination showed perivascular infiltration of round cells in the superficial and the deep layers of the cutis. Several small vessels contained hyaline thrombi. Severe intercellular edema was present in some areas at the basal layer, and in this region there was some liquefaction necrosis of the basement membrane and of the adjacent fibrous tissue of the cutis. These changes suggested the diagnosis of lupus erythematosus.

DISCUSSION

DR. HENRY SILVER: About a year ago I presented before this society a case of the so-called Senear-Usher syndrome (ARCH. DERMAT. & SYPH. **41**:808 [April] 1940) with the view of clearing the controversy over this syndrome. It was agreed in the discussion which followed that there is not enough clinical or histologic evidence to warrant the separation of this syndrome as a clinical entity. The conditions described under the name Senear-Usher syndrome are confusing

and could, in the light of newer knowledge, be identified clinically as lupus erythematosus, bullous lupus erythematosus, benign pemphigus or pemphigus vulgaris.

Dr. Astrachan's case illustrates the points raised. Since the condition lacks the classic symptoms of pemphigus, the diagnosis of Senear-Usher syndrome is suggested by the presenter. Yet there are, in my opinion, enough clinical symptoms, including the Nikolsky sign, to establish with reasonable certainty the diagnosis of pemphigus. The absence of lesions of the mucous membranes does not militate against that diagnosis.

DR. WILBERT SACHS: From the sections that I examined it is difficult to make definite statements. There were no features of lupus erythematosus or of pemphigus. There was a superficial dermatitis with a superadded acute toxic bullous lesion not unlike that seen in epidermolysis bullosa. Such a process would fit in with the picture of Senear-Usher syndrome.

DR. PAUL GROSS: It is my firm belief that the description of the Senear-Usher syndrome has been an outstanding contribution to dermatology, since it differentiates a condition which is neither lupus erythematosus nor pemphigus vulgaris. The disease is a benign bullous eruption involving particularly the face, chest and back, with lesions that are persistent and show a tendency to enlarge. Although the condition is chronic, it may disappear after several years. There is nothing known about the cause, and there is no relation to lupus erythematosus.

DR. ADOLPH ROSTENBERG: I believe that the condition in this case represents the condition known as benign pemphigus.

DR. LOUIS CHARGIN: My impression is that what Senear and Usher originally described was not a clinical entity but a bullous eruption with features of pemphigus and of lupus erythematosus, yet it did not seem to fully fit into either one. More recently they have admitted that the syndrome is not lupus erythematosus. Before the condition described by Senear and Usher is established as a clinical entity, there should be more evidence than there is now. The condition in the case presented does not impress me as the so-called Senear-Usher syndrome or as a definite example of lupus erythematosus. The Senear-Usher syndrome presents clinically noninflammatory lesions that are seborrhea-like, and there is no stormy history such as in this case. I should rather label this case one of a form of toxic erythema with bullous lesions.

DR. HERMAN SHARLIT: I am inclined to agree with Dr. Chargin that there is no need for calling the condition in this case pemphigus or lupus erythematosus. However, the discussion has come around to the point of trying to agree as to what Senear and Usher had in mind. It is interesting to note that the older Jadassohn said, in a footnote in his textbook (Jadassohn, J.: Dermatologie, Weidmann & Co., Vienna, 1938, p. 632), that the American dermatologists called the bullous form of lupus erythematosus the Senear-Usher syndrome; that, at least, was his impression of the meaning of syndrome.

DR. SAMUEL FELDMAN: The conception of pemphigus needs to be modified. Up to the present I have encountered cases in which the disease began with inflammatory lesions which could not be diagnosed as pemphigus. After two to three weeks the inflammation subsided and clear bullae remained. This does occur, and yet it does not necessarily exclude pemphigus. Dr. Sachs reports, with regard to the case presented, that histologically the lesions do not suggest pemphigus. This, of course, is a point against the diagnosis. However, clinically the condition may still be pemphigus.

DR. HENRY SILVER: Senear and Usher described a combination of pemphigus with features of lupus erythematosus (including features of seborrheic dermatitis). Later there appeared in the literature reports of a condition typical of lupus erythematosus with bullous lesions, and this was also called the Senear-Usher syndrome. From then on it was not clear whether the Senear-Usher syndrome was

lupus erythematosus, pemphigus or a combination of both. Recently Senear himself admitted the existing confusion and was inclined to consider this condition as a variant of pemphigus.

DR. FRANK E. CROSS: From the standpoint of prognosis it is important to distinguish between the benign type of pemphigus and the pemphigus which is so common among Russian Jews and is usually fatal. This man's condition does not impress me as pemphigus vulgaris. A patient with this condition is sick; his facies shows it, and he has a feeling of impending death.

DR. GIRSCH D. ASTRACHAN: I showed the slides in this case to Dr. Satenstein and to Dr. Sachs, and they both maintained that the histologic picture does not show any evidence of either lupus erythematosus or pemphigus. One feature in this case, the sudden flare-up of the lesions with rapid changes in the clinical picture, is worth stressing. This factor was characterized by Senear (in discussion on Wile, U. J., and Arnold, H. L., Jr.: The Senear-Usher Syndrome: Review of the Literature and Report of Six Cases, ARCH. DERMAT. & SYPH. **40**:704 [Nov.] 1939) as an important clinical element in many cases of Senear-Usher syndrome. However, I have to agree with Dr. Silver that this case may eventually prove to be one of pemphigus.

A Case for Diagnosis (Necrotic Ulcers). Presented by DR. FRANK E. CROSS.

I. W., a German housewife aged 65, was first seen on Jan. 21, 1941, with a linear sharply defined crusted lesion on the outer posterior surface of the upper third of the right arm. The lesion was about 6 by 2 cm. in size with the crust on a level with the skin. The lesion was discovered accidentally by the patient while drying the arm with a towel. There is no history of trauma, ingestion of drugs or application of medicaments. About one and a half years ago there appeared a similar, somewhat larger lesion, which was not diagnosed at that time. The area healed in about two months, leaving a keloidal scar over the right scapular region.

DISCUSSION

DR. CHARLES LERNER: Before a definite diagnosis in this case is attempted, tests for loss of pain sensation and temperature are necessary. It would be difficult for the patient to incur a burn of this extent without realizing it. If pain and temperature sensations are normal, the condition may be hysteria; if they are abnormal, a neurotrophic disturbance must be considered.

DR. ADOLPH ROSTENBERG: The appearance of the lesion suggests an artefact. It does not fit the description of a trophic disturbance like syringomyelia. Trophic changes in the hands, such as atrophy of the interosseus muscles and ulcerations on the fingers, are lacking.

DR. HENRY SILVER: Is there additional information as to the mental makeup of this patient?

DR. ARTHUR SAYER: I think it important that serologic examination of the blood and spinal fluid be made. I do not think the patient has syringomyelia, because symptoms of this disease are bilateral. The woman has a definite anesthesia on the right side only and also weakening of the muscles of the arm on that side. This would speak rather in favor of a lesion of the lower part of the cervical region of the cord, possibly a gumma involving the lower right cervical nerve roots.

DR. FRANK E. CROSS: In answer to Dr. Silver, I wish to say that I know the patient and the family well enough to know that there are no neuropathic tendencies present. Dr. Lerner's point is well taken. There was a disturbance of sensation on the right side of the chest and back and the right arm. After I had established this sensory disturbance the patient admitted that about two years previously she had had Bell's palsy on the right side of the face, which had cleared with diathermy treatment. I cannot agree that the lesion followed a burn.

In all probability the patient presents a trophic ulcer. In answer to Dr. Sayer, the Wassermann reaction one year ago was negative.

Pityriasis Rubra Pilaris with Psoriasis-Like Lesions. Presented by DR. SAMUEL FELDMAN.

M. R., an American-born man aged 33, a plasterer, was referred for an opinion because of supposedly occupational dermatitis due to plaster of paris. The patient stated that early in December 1940 he noticed red "blotches" on the face, palms and soles. The lesions on other parts of the body appeared later. The eruption was not accompanied by itching. The only discomfort the patient complained of was stiffness of the hands, which made it difficult for him to follow his occupation.

There are bright red, shiny, slightly elevated, confluent patches on the forehead. The palms and soles are red, and the skin is firm, thickened and hyperkeratotic and feels like thick parchment. On the backs of the fingers and on the arms, forearms and thighs there are red follicular papules capped by horny plugs. A number of red patches similar to those on the face are found on the upper extremities. Scattered over the chest, back and arms there are a number of small red patches, about 2 cm. in circumference, covered with dry scales, not unlike those seen in psoriasis. On the elbows and knees there are thick infiltrated patches; these preceded the generalized eruption.

The face and palms were treated with roentgen rays once weekly. The patient received liver and stomach extract with iron (lextron), 6 capsules a day. The condition began to improve after the first week. The improvement was not localized to the areas which were exposed to the roentgen rays.

DISCUSSION

DR. VAN ALSTYNE H. CORNELL: The patient presents the characteristic pinpoint-sized horny blackish papules on the phalanges. Some of the lesions on the trunk resemble psoriasis. The patient also gives a history of having had seborrhea of the scalp, which was probably associated with his present condition. I agree with the presenter's diagnosis.

DR. ADOLPH ROSTENBERG: In connection with this case, I should like to report an observation I recently made in a case of pityriasis rubra pilaris in a girl of 12 years. The patient was under my observation for several months and presented a typical picture of that disease. During an intercurrent illness she had received sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine). There appeared a severe toxic eruption of an urticarial type, which is occasionally encountered with this drug. The rash persisted for a few weeks, and when it cleared the manifestations of pityriasis rubra pilaris had disappeared as well.

DR. ARTHUR SAYER: The patient claimed that the eruption developed as a result of his work. The presenter states that the patient had definite clinical signs of pityriasis rubra pilaris, and therefore he rejected the patient's claim for compensation. There is no doubt that clinically the man has keratosis of the hands, palms and feet and plaques on the phalanges which would warrant the diagnosis of pityriasis rubra pilaris. One must not eliminate, however, the possibility that a patient with pityriasis rubra pilaris may also have an occupational dermatitis. He is a plasterer by trade and comes in contact with irritating materials which may cause a dermatitis. In view of the fact that the condition cleared within six weeks, there is the added possibility that the generalized dermatitis may have been due to his work, since pityriasis rubra pilaris is usually persistent in spite of all treatment.

DR. CHARLES LERNER: I am inclined to share Dr. Sayer's opinion. One of my patients was ready to bring suit against a prominent paint-manufacturing corporation because he had pityriasis rubra pilaris which developed rapidly after he handled a freshly opened can of paint. The history and the clinical picture presented by my patient resembled closely those in the case presented by Dr.

Feldman. It is, of course, difficult to determine whether some ingredient in paint may start the symptom complex that is called pityriasis rubra pilaris.

DR. SAMUEL FELDMAN: The question of compensation is for the commission to decide. In my opinion there is no dermatitis venenata present. The condition is clearcut pityriasis rubra pilaris. It began to clear up after small doses of vitamin because the disease was rather recent.

A Case for Diagnosis (Psoriasis?). Presented by DR. HARRY B. FEILER.

E. J. H., a girl aged 4 years, was first seen in August 1940. She presented a condition of the palms and soles resembling pityriasis rubra pilaris. The skin in the affected areas was parchment-like and dusky red. There were no other lesions on the body.

The mother stated that the hands and feet became involved during the middle of that summer. She thought the child may have been "burned" by lime while playing near a building under construction.

Early in December 1940 the patient presented lesions on the knees suggestive of psoriasis. Two weeks later similar lesions appeared on the elbows.

DISCUSSION

DR. CHARLES LERNER: I think that the condition is pityriasis rubra pilaris.

DR. PAUL GROSS: The diffuse keratosis of the palms seems to be more suggestive of localized pityriasis rubra pilaris than of psoriasis. I have seen palmar and plantar keratosis in other cases, as well as typical pityriasis rubra pilaris, respond to treatment with vitamin B complex. Only recently I saw a young woman with a keratosis confined to the palms which failed to respond to intermittent treatment with nicotinic acid and riboflavin. After more intensive therapy with intramuscular injections of liver extract, the general condition improved and the lesions on the palms almost disappeared. In view of my experience in cases of this kind I advise liver therapy for this child's condition. After more than six years of clinical investigation, I have found a limited number of eruptions responding readily and completely to injections of liver extract. The number of such cases may increase when a natural vitamin B complex of high potency becomes available for parenteral use.

DR. LOUIS CHARGIN: I think the evidence warrants a diagnosis of pityriasis rubra pilaris, because one does not often see the entire palm affected with psoriasis. I recall a child in whom the disease disappeared in six weeks. I also saw an adult suffering from syphilis and pityriasis rubra pilaris with a similar result. As to the suggestion of Dr. Gross, by all means this child should be treated with vitamins; one should, however, bear in mind that the disease clears spontaneously.

DR. HARRY B. FEILER: This child has had several episodes of pneumonia, and the eruption followed the last attack. It is possible that sulfanilamide, so frequently used for pneumonia, may be a factor in the production of the disease. I have given the child liver extract by mouth for the past two months in moderate doses. There has been little response so far.

Granuloma Annulare. Presented by DR. LEO SPIEGEL.

S. K., a white man aged 54, a baker, presents an eruption of about one year's duration. He states that he has had neither gonorrhea nor syphilis. There is no history of ingestion of drugs which could be responsible for the appearance of the lesions. There were no subjective symptoms. The patient is well developed, well nourished and apparently in good health.

The lesions are symmetrically placed on the sides of the neck. Besides, a small nodule, about 1 cm. in diameter, is situated on the bridge of the nose; it is annular, purplish and button-like. This lesion appeared much later than the larger ones. The lesions on the sides of the neck consist of two complete inter-

locking ovals or rings forming a figure 8, each ring about 4 cm. in diameter. These annular lesions are well defined, reddish brown, raised, smooth, cordlike and firm to the touch. The skin in the centers of the lesions appears paler and whiter. It is, however, not atrophic in comparison with the skin of the outer side of the rings.

A roentgenogram of the chest revealed a partially calcified scar in the right infraclavicular region. There was some calcium deposited in the nodes of the right hilus. Thickened bronchovascular markings were noted in the lower portions of the lungs. Some peribronchial infiltration was present at the base of the left lung. The cardiac shadow was not enlarged.

The tuberculin test (Mantoux) elicited positive reactions with dilutions of 1:100,000 and 1:50,000 and a negative reaction with a dilution of 1:1,000,000. The urine was normal. The Wassermann reaction was negative with both alcoholic and cholesterolized antigens. The Kline flocculation test also gave negative results with both diagnostic and exclusion antigens.

Histologic examination of sections stained with Ziehl-Nielsen stain showed no acid-fast bacilli. The entire corium was involved, showing edematous, streaky, thickened strands of collagen extending longitudinally through areas of infiltration which varied in size. These areas were perivascular, perifollicular and periglandular and consisted of stellate and elongated mononuclear cells in a lacy and alternatingly dense reticulum.

DISCUSSION

DR. LOUIS CHARGIN: In granuloma annulare one usually sees nodules which have a tendency to form circles and are whitish or ivory in color; they have definite clear centers. In this case there is a similar border, but individual nodules are lacking. The lesions with reddish or bluish centers are different clinically from those seen in granuloma annulare. At the last session of the American Academy of Dermatology and Syphilology cases of this type were presented as instances of lipoidosis. In view of this I suggest that the case be studied from this standpoint.

DR. WILBERT SACHS: I wish to recall in this connection Dr. Traub's case in which histologic sections showed many giant cells, no granular degeneration and the presence of fat. In granuloma annulare one sees granular degeneration, few giant cells and no fat. Dr. Weidman and others agreed with the diagnosis. In Dr. Spiegel's case the rings are small, and I could not see the individual lesions making up the circles. However, the histologic features in this case are those of granuloma annulare. The process is in the upper and middle parts of the cutis, not in the deep portion or in the fat, and there are granular degeneration, few if any giant cells and many epithelioid cells, some in tubercle formation.

DR. LEO SPIEGEL: Lesions of this kind are often diagnosed as xanthoma. The interesting points in this case are the age of the patient, the few lesions present and the probability that the underlying cause is pulmonary tuberculosis.

Kaposi's Sarcoma with Involvement of the Eye. Presented by DR. HENRY SILVER.

J. B., an Austrian Jew aged 84, has been suffering from diabetes and asthma for many years. In 1925 he came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital presenting a lesion on the face which was diagnosed as epithelioma and for which he received roentgen ray treatment. In 1929 he was treated at the department of radiotherapy of Mount Sinai Hospital for keratoses on the right temple and in the right malar region. Some of these lesions were electrodesiccated. In 1930, 1934 and 1936 he had recurrences of the lesions on the temple and nose. In March 1938 the patient underwent an operation for bilateral cataract. Nine months later conjunctivitis developed with a purulent discharge, which improved under treatment. In August 1938 the patient was

referred to the department of dermatology (outpatient department) at Mount Sinai Hospital because of numerous nodular lesions on the right leg and forearms. In November 1940 a red hemorrhagic cyst developed in the right lower conjunctival sac. The patient was referred to the department of ophthalmology and was operated on in January 1941. The tumor was examined histologically and reported as angiosarcoma.

On the arms and legs there are scattered, raised, erythematous nodules ranging in size from that of a pea to that of a cherry. Some lesions are definitely indurated; others are soft and hemorrhagic. On the left forearm and hand there appeared recently a group of raised purplish red lesions. A number of lesions on the leg healed, leaving depressed scars.

The Wassermann reaction was negative. Urinalysis showed the presence of sugar. The histologic examination of one of the cutaneous lesions showed Kaposi's sarcoma.

DISCUSSION

DR. CHARLES WOLF: The interesting feature in this case is the site of the involvement. Kaposi's sarcoma occurs in various organs. I have never seen a lesion on the conjunctiva before. The ophthalmologist should be informed that angiosarcoma is a part of the picture of Kaposi's sarcoma.

DR. SAMUEL FELDMAN: I presented a patient before the New York Academy of Medicine, Section of Dermatology and Syphilis (ARCH. DERMAT. & SYPH. **27**:692 [April] 1933), as well as before this society (ibid. **27**:364 [Feb.] 1933), whose condition had begun with a small papule on the palate. When I removed the lesion and sectioned it I found the histologic picture to be typical of Kaposi's sarcoma. There was, of course, disagreement with the diagnosis because of the one small lesion. The patient later had a lesion on the eyelid. It cleared with roentgen ray treatment but subsequently recurred.

DR. WILBERT SACHS: Kaposi's sarcoma is a type of angiosarcoma, and in some stages the two conditions cannot be differentiated. I can readily understand how such a diagnosis was suggested.

DR. HENRY SILVER: The involvement of the eye in Kaposi's sarcoma is rare. For a long time it was thought that lesions in Kaposi's sarcoma were limited to the lower extremities, and such names as acrosarcomatosis and acroperitheliomas were suggested. Unusual locations, however, such as the scalp, the face or the mouth, have been recorded. Dr. Feldman's case, with a solitary lesion on the hard palate, is an instance of this condition. It is, of course, difficult for physicians in other specialties to diagnose the disease correctly. In this patient the lesion of the conjunctiva was removed and diagnosed as angiosarcoma by an ophthalmologist, which is pretty close. From the days of Kaposi until now this disease has eluded a satisfactory solution. The interpretations were based mainly on histologic studies. MacKee and Cipollaro (*Am. J. Cancer* **26**:1-28, 1936) pointed out that the histologic picture is often that of a sarcoma. This, however, does not establish the disease as such because clinically it does not behave like a sarcoma. That histologic examination alone cannot yield a final solution of the problem is evidenced by the many types of cells which are arranged along the capillaries, i. e., fibroblasts, histiocytes, mast cells and plasma cells.

Lichen Planopilaris (Lichen Planus et Acuminatus). Presented by DR. MAURICE UMANSKY.

F. B., a woman aged 55, presents a moderately itchy eruption of seven months' duration. The patient is well nourished and weighs 167 pounds (75.7 Kg.). She suffers from mild diabetes.

The eruption involves the trunk and the extremities. The back and the posterior surfaces of the shoulders are mostly affected. Two types of lesions are noted. One type consists of glistening, miliary, flat-topped, angulated papules;

the other type, of lesions the size of a pea which show a central pigmented depression and an annular border. The vast majority of the papules belong to the second type. They are either discrete or grouped follicular acuminate and conical papules; some show horny filiform projections. The color of the lesions is that of normal skin or slightly pinkish. Linear arrangement of the papules can be seen in some areas. The surface of the skin has a nutmeg-grater-like feel.

The urine has recently been free of sugar. The chemical examination of the blood showed 38 mg. of nonprotein nitrogen and 177 to 200 mg. of sugar per hundred cubic centimeters. The Wassermann reaction was negative. Mantoux tests with dilutions of 1:1,000,000, 1:100,000 and 1:10,000 of old tuberculin gave negative reactions; with a dilution of 1:1,000 a slightly positive reaction was elicited.

Roentgenograms of the chest and hands showed no pathologic changes. Histologic examination (Dr. S. Peck) of a section taken from an annular lesion showed lichen planus. Examination of a follicular lesion showed the inflammatory reaction to be almost entirely around the hair follicle. The exudate consisted of many plasma cells and large histiocytes resembling epithelioid cells. No definite diagnosis could be established.

DISCUSSION

Dr. Samuel Feldman: This case is extremely interesting. Clinically the condition resembles lichen planus and acuminatus atrophicans which I described; however, it lacks the atrophic lesions. I recall a case in which the atrophy developed later in the course of the disease. An unusual feature in this case was the presence of the histiocytes. As a rule infiltration is around the mouth of the follicle, while in this case one cannot determine the exact location.

Dr. Maurice Umansky: Clinically, the patient shows flat and spinulous lesions. Pringle felt that the designation lichen planus, which indicates the flatness of the lesions, is not the proper one for the condition in question and called it lichen planopilaris. The name lichen planus et acuminatus has the disadvantage that it may be confused with lichen acuminatus, which is reserved in German literature for the acute, malignant and fatal form of pityriasis rubra pilaris. Histologic examination of an excised follicular acuminated lesion did not reveal any elements of lichen planus. The presence of histiocyte-like cells, plasma and giant cells makes the interpretation of the slides difficult.

Lupus Vulgaris Treated with Pyrogallol. Presented by Dr. Charles Lerner.

Mrs. C. G., aged 45, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in September 1939. Two years later there developed, fairly rapidly, an eruption on the nose, proved by histologic examination to be lupus vulgaris.

Examination at that time revealed disseminated, small, nodular, erythematous, ham-colored lesions on the bulb of the nose; on the bridge of the nose there were a few scattered lesions. There was no evidence of scarring. The lesions had already extended to the nares and glabella. Diascopic pressure revealed characteristic apple jelly nodules.

The Wassermann and Kahn reactions were negative. The blood count showed 4,370,000 red blood cells and 4,900 white blood cells, with 66 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 3 per cent monocytes and 29 per cent lymphocytes; there was 76 per cent hemoglobin. The urine was normal. Roentgenographic examination of the thorax showed small patches of second stage tuberculous infiltration of both apexes.

Roentgen therapy, irradiation with a water-cooled quartz mercury vapor arc lamp with pressure, a high vitamin and salt-free diet and other therapeutic measures had been used with little success.

This case is presented for the sole purpose of showing a good result obtained with 20 per cent pyrogallol ointment. Most patients cannot stand this strength

applied for any length of time. This patient has shown willingness and ability to withstand considerable pain.

DISCUSSION

DR. HENRY SILVER: Treatment with pyrogallol is not new. The late Dr. Goldenberg, of Mount Sinai Hospital, was partial to the drug and used it particularly in children. For individual lesions one obtains good results.

DR. PAUL GROSS: The treatment with pyrogallol in this case should be considered only a preparatory measure for ultraviolet radiation compression treatment and for general measures like salt-free diet and heliotherapy.

DR. ARTHUR SAYER: What is the presenter's technic in applying the pyrogallol?

DR. CHARLES LERNER: The patient is instructed to apply petrolatum to the healthy skin up to an area about ½ inch (1.3 cm.) away from the diseased tissue. Then the 20 per cent pyrogallol ointment is applied to the affected region.

Pityriasis Lichenoides Chronica with Varioliform Lesions. Presented by DR. CHARLES WOLF.

A. S., a man aged 20, has had excellent health except for this eruption. Three siblings are well. There are no constitutional diseases in the family.

The eruption first appeared about two years ago on the upper part of the body, involving the chest and arms. It spread downward to the sides of the chest. At present it involves the loins, buttocks and thighs. It consists of flat, scaly, pale pinkish, irregularly shaped lesions. There is no subjective complaint. In addition, on various parts of the body there are varicella-like lesions which have a tendency to heal spontaneously.

The Wassermann reaction was negative.

LEO SPIEGEL, M.D., *President*

HENRY SILVER, M.D., *Secretary*

Feb. 27, 1941

Pruritus Senilis Treated with Testosterone Propionate. Presented by DR. SAMUEL FELDMAN.

M. F., a Russian Jew aged 86, was admitted to the Home of the Daughters of Jacob in 1939. He was in comparative good health, was married and had eight children. He had suffered from generalized pruritus for many years. In the beginning there had been short periods of remission, but the itching had become severe and persistent and was most pronounced on the lower extremities. The patient appeared well preserved for his age, and his mental processes were excellent.

On Oct. 15, 1940 the skin appeared considerably thinned, shiny and unduly wrinkled. There was considerable loss of elasticity. Scratch marks were present. Laboratory examinations of the blood and urine and chemical examination of the blood showed no abnormalities.

On October 19 treatment with testosterone propionate was instituted. Following two subcutaneous injections of 10 mg. no change was noted. On November 4 5 mg. of the androgen was injected, following which there was substantial amelioration of the itching. The smaller dose was repeated every five days until Jan. 11, 1941, at which time the itching, except for an occasional mild pruritus of the legs, had disappeared.

Histologic examination of a specimen taken before treatment showed a thin epidermis of two to four layers and disappearance of the papillae and of the rete pegs. The corium was thinned and edematous. The collagenous bundles were

widely separated, had lost their normal, orderly arrangement and were scattered in an irregular manner. The elastic fibers were fractioned and clumpy. The biopsy specimen taken after the treatment was given showed considerable reversion to normal. The layers of the epidermis were increased in number from four to seven; the edema was diminished, and the collagenous bundles were normal in both appearance and arrangement. The changes in the elastic tissue were less pronounced.

Pruritus Senilis Treated with Testosterone Propionate and Estradiol Benzoate. Presented by DR. SAMUEL FELDMAN.

M. F., a Russian Jewish housewife aged 82, was admitted to the Home of the Daughters of Jacob in December 1939. She had suffered from generalized pruritus for many years. During the previous two years the itching had become intense, especially in the genital region. The patient had five children, and the last menstrual period was at the age of 50. Physical examination revealed arteriosclerosis and chronic myocarditis. The skin appeared loose, wrinkled, thin and slightly scaly. There were few scratch marks. The vaginal tract was smooth, pearly white and dry.

On Sept. 25, 1940 the condition and appearance of the skin and of the vulva were about the same as on admission. Vaginal smears showed occasional epithelial cells with small nuclei and mainly white blood cells. The urine was normal. The chemical examination of the blood showed no abnormalities.

On Sept. 30, 1940 10 mg. of testosterone propionate were injected subcutaneously. The dose was repeated every five days until November 4 without apparent improvement in either the generalized itching or the genital pruritus. Examination of vaginal smears showed the same picture as on September 25. Treatment with testosterone was discontinued, and estradiol benzoate, an estrogen, was substituted. It was given in doses of 1 mg. subcutaneously every five days. After two injections the itching of the skin and genitals was greatly improved. On November 25, three weeks after the change in treatment, the itching had entirely disappeared. The treatment was continued once a week with injections of 1 mg. of the estrogen. On December 25 a vaginal smear showed numerous epithelial cells with large nuclei and only an occasional leukocyte. On Jan. 11, 1941 the patient was entirely free of symptoms.

A specimen of skin was taken before treatment was instituted. A second specimen was taken after treatment about 1 inch (2.5 cm.) away from the site of the first biopsy specimen. The histologic examination showed changes similar to, only perhaps less conspicuous than, those described in the first case presented.

DISCUSSION OF CASES OF PRURITUS SENILIS

DR. SAMUEL FELDMAN: My experience with pruritus vulvae and early kraurosis with glandular extracts led me to treat senile degeneration with endocrine substances. I therefore instituted this treatment in cases of senile pruritus. I observed that after two or three injections of 5 or 10 mg. of testosterone propionate, the itching was ameliorated and then completely disappeared. After two months all but 1 patient was free from itching. To date there have been no recurrences. I do not claim that these patients are cured, because in the absence of the endocrine secretion the pathologic changes which ensue must recur unless the substance is constantly supplied. These patients, however, can be kept free from itching. The sex hormones closely resemble each other and are known as steroids. A close relative of the androgen testosterone is found in the urine of females almost as commonly as in that of males. That made me think of the possibility of obtaining the same reaction with testosterone in both sexes. However, after five injections of testosterone propionate failed to relieve 2 women, the treatment was changed to estrogen; after a few injections the itching stopped, and the patients are now free from pruritus. The pathologic observations in these cases are even

more remarkable. In all of them the skin was atrophic and highly edematous before treatment, and there was a decided reversion to normal after the treatment to such an extent that when the eight sets of slides were shown to Dr. W. Sachs, he was able to pick out which specimen was taken before and which after treatment.

Dr. J. H. Pollack is collaborating with me in this work.

Dr. Julius H. Pollack (by invitation): In male patients we began with the use of 10 mg. of testosterone proprionate, which is comparable to the dose used in other fields of endocrine therapy. This dose was given every five days and later was reduced to 5 mg., which was given once a week. This was a sufficient dose to keep the patients free from itching. The women were given 1 mg. of estradiol benzoate once a week. In 1 case after four days and in another case one week after the injection there was a definite diminution of the itching. Two patients had senile vulvovaginitis, and this condition was also considerably benefited.

One case merits special mention. A man had been treated for severe generalized pruritus for two years with a variety of remedies, including roentgen ray therapy. When the patient came under our observation he was suffering from a severe dermatitis with hyperpigmentation and lichenification. Treatment was instituted in the manner described, and after ten days the itching was greatly diminished. In two weeks the hyperpigmentation and the subacute dermatitis cleared to such degree that the contrast was striking.

Most patients with this condition complain of itching of the lower extremities, and it is difficult to effect complete disappearance of the pruritus in these parts. This is especially true when the patient's limbs have definite circulatory disturbances with hypostatic edema. We are under the impression that in such instances factors other than the endocrines are operative.

Dr. Wilbert Sachs: From a cursory examination of the sections presented I was able to tell which tissue was taken before and which after therapy. In 1 instance the epidermis led me to state which tissue was more normal, and in another the cutis; in other words, it was not always the same portion of the skin which gave the clue. I understand that there are special features in the blood vessels to be observed, which I have not yet had time to study.

Dr. Paul Gross: The results obtained by Dr. Feldman are encouraging, but it seems to me that the man presented still shows evidence of a vitamin A deficiency, consisting of scattered follicular keratotic papules on the arms and a diffuse dryness and chapping of the hands. It would be interesting to study the effect of the testosterone injections on the creatine-creatinine excretion in the urine.

Dr. Samuel M. Peck: Dr. Feldman and his co-workers are to be congratulated for their excellent demonstration. It is only in the older women with definite local changes which can be shown by vaginal smears that the administration of estrogens helps pruritus vulvae. Of importance is the fact that large doses over a long period must be given. Almost the same can be said of vitamin A therapy. There must be a definite indication either clinically or based on studies of the blood or visual changes before vitamin A is given. If a definite deficiency has been found the results will be satisfactory. This substance also must be given in large doses over long periods. Probably in many instances one will find an endocrine disturbance and a vitamin deficiency in the same case, both of which must be taken care of to obtain adequate results.

Dr. Adolph Rostenberg: Pruritus senilis is without a doubt one of the dermatoses most rebellious to treatment, and any promising remedy should be greatly welcomed. I have not been as fortunate as Dr. Feldman. I have tried endocrine principles in old and young patients, and if there was slight improvement for a short time, I was inclined to ascribe it more to mental stimulation, as any new method of treatment is apt to help at first. Sex in old people seems to me problematic, as the sex organs have become atrophic and can hardly be restored to resume their functions.

DR. HERMAN SHARLIT: In women during the menopause, during which generalized itching may be an essential symptom, the estrogenic substances are effective. I have had occasion, before androgen was available, to use estrogen in elderly men who had itching and have obtained good results. I think Dr. Rostenberg's suggestion that one must not overlook the psychic approach to pruritus is a good one, but, of course, if one treats a large series of senile men, one is bound to get better results with the estrogens than when using just a hypodermic needle.

DR. SAMUEL FELDMAN: Dr. Gross's suggestion is well taken. We are planning to study the creatine excretion. The cholesterol content and the sugar content of the blood have been studied and found normal. We have of course attempted to keep a check on our patients, and the results have been gratifying thus far. There is an inmate in a home for the aged who has been annoying every one at the hospital for about eighteen years, begging for relief from his itching. Needless to say, a variety of treatments was given without success. After the second injection of testosterone proprionate, the patient felt relieved for the first time. He had never reacted in this manner to any of the previous medications. The specificity of the drug has been questioned. When one takes into account the 2 women who showed no improvement with testosterone and who reacted promptly to estrogen, one should be convinced. Yet, we have begun new control studies, and patients with pruritus are now receiving injections of sesame oil, the medium in which the endocrine substances are dissolved.

Dr. Rostenberg should not be concerned about the possibility that one may not be able to regenerate an atrophied testicle. In spite of the fact that testosterone is known to increase spermatogenesis in a poorly functioning testicle, no action on the testes in the aged is claimed. At the outset I stated that we do not consider this treatment a cure. Something is being supplied, however, which is needed to maintain certain body functions, in the same manner as insulin does not cure diabetes but supplies something which a diseased pancreas is unable to furnish. To prove the efficiency of the drugs, one has only to examine the tissue before and after treatment. There are definite pathologic changes in senile skins, and there is a decided improvement in the pathologic process after the treatment.

Necrobiosis Lipoidica Diabeticorum in a Nondiabetic Person. Presented by DR. WILLIAM LEIFER.

M. S., a woman aged 35, was admitted to the clinic of the Mount Sinai Hospital in December 1940 because of lesions on the legs which had appeared first about four years previously as small red spots and had gradually increased in size. There were no subjective symptoms.

The patient has been married nineteen years, has been pregnant four times, all offspring being alive and well. There is no history of serious illness at any time in her life. The mother had mild diabetes at the age of 60, which was controlled by diet without insulin. Her father is nondiabetic, and there are no siblings.

The eruption is confined to the anterior aspect of the upper half of the legs. On the left leg there are four and on the right leg three well developed lesions. Several incipient lesions are present on both legs. The characteristic lesions are the size of a coin, slightly elevated, flat, firm and not tender; they are plaquelike, have a smooth shining surface without growth of hair and are traversed by telangiectatic vessels. The central portion is somewhat yellowish, while the border is reddish and well demarcated; outside the border of some of the lesions is a faint violaceous halo.

The Wassermann reaction was negative. Repeated examinations of the urine gave negative results. The cholesterol content of the blood was 205 mg. per hundred cubic centimeters. The results of a dextrose tolerance test (Janney) were within the limits of normal. A complete blood count revealed no abnormalities.

Histologic examination of tissue removed from one of the lesions showed that the epidermis was atrophic and reduced to a few layers. The papillary bodies were flattened. Directly under the epidermis, separated by only a narrow band of collagen, were areas of infiltration arranged in fairly circumscribed masses extending to about the midcutis. These areas consisted of dilated blood vessels and masses of lymphocytes. The collagen showed considerable degeneration, taking a basophilic stain. The elastic tissue was absent except for a few small fragments in the papillary and subpapillary bodies. In these areas of infiltration both elastic tissue and collagen fibers were not seen, except as isolated fragments. With a sudan stain no fat was demonstrable in the diseased areas. The histologic examination showed that there was evidently a necrotic degenerative process. A diagnosis of necrobiosis lipoidica diabeticorum, as described by Urbach, could not be established unless the demonstration of fat droplets was not essential.

DISCUSSION

DR. SAMUEL M. PECK: The second biopsy specimen also failed to show extracellular fat and was similar in all respects to the first specimen.

DR. WILBERT SACHS: Necrobiosis lipoidica may or may not be associated with diabetes. The histologic picture described does not suggest either type of necrobiosis lipoidica.

DR. CHARLES WOLF: I believe the process is not necrobiosis lipoidica and offer the diagnosis of scleroderma. The histologic observations of degeneration and replacement of connective tissue and atrophic epidermis suggest scleroderma in the edematous stage.

DR. HENRY SILVER: At the last meeting of the Academy of Dermatology and Syphilology, held in Chicago, Dr. Oppenheim showed a moulage demonstrating lesions on the lower extremities closely resembling the lesions seen in this case. He described this entity under the name of dermatitis atrophicans lipoidica diabeticorum. Dr. Gross presented a similar case in 1934 as one of morphea with xanthomatous infiltration; the condition was later recognized as necrobiosis without diabetes (ARCH. DERMAT. & SYPH. **30**:598 [Oct.] 1934). Clinically the lesions differ from those described by Urbach. The lack of lipoid infiltration of the tissue should be stressed. However, similar cases are on record.

DR. GIRSCH D. ASTRACHAN: I have recently observed a case of necrobiosis lipoidica, with the diagnosis proved histologically by Dr. Sachs, in which, too, there was no evidence of diabetes.

DR. LOUIS CHARGIN: I am convinced that on clinical grounds alone this condition is necrobiosis lipoidica in a nondiabetic person. Cases of this kind have been on record. Whether the name necrobiosis lipoidica is correctly given is another matter. The lesions began with small red papules which gradually assumed their present character. That is the exact clinical description of the disease, and it is not necessary always to find fat histologically. Also, an important consideration is the fact that the specimen for biopsy should have been taken from the center of the lesion, not from the border, because it is in this location that the fat is commonly found.

DR. PAUL GROSS: This case is an important one to follow; particularly it would be well to carry out Dr. Chargin's suggestion to take the biopsy specimen from the center of the lesion. Clinically the condition is suggestive of necrobiosis lipoidica, and one lesion on the right leg shows a lemon-colored discoloration in the center which becomes more distinct on pressure.

DR. WILLIAM LEIFER: From the Mayo Clinic a report was published (Hildebrand, A. G.; Montgomery, H., and Rynearson, E. H.: *Arch. Int. Med.* **66**:851-878 [Oct.] 1940) of 8 cases of this condition, with a review of 78 previously reported cases in the literature. In only 8 of the 86 cases the condition was not associated with diabetes. In another case, reported by Belote and Welton (ARCH.

DERMAT. & SYPH. **40**:887-896 [Dec.] 1939), the patient was also nondiabetic. In a case similar to the one presented there were characteristic histologic changes, except that no lipoid could be demonstrated (Bruce-Jones, D. B. S.: *Brit. J. Dermat.* **49**:238-240, 1937).

I think it important to emphasize that this woman's mother had diabetes. It is known, of course, that diabetes is definitely a familial disease. It may be that this condition can occur prediabetically in some persons.

Dermatomyositis. Presented by DR. MARION B. SULZBERGER.

M. G., aged 31, a plumber, was admitted to the Montefiore Hospital for Chronic Diseases on Jan. 3, 1941. He complained of dull aching pains, swelling and tenderness of the finger joints, wrists, elbows, shoulders, knees, ankles and toes. There was immobility of some of the joints because of extreme tenderness and pain. Fever was associated with these symptoms. There was puffiness and swelling of the lower lids and the adjacent maxillary region, which were worse in the morning and decreased during the day. There was also some difficulty in swallowing. During the same period erythematous patches appeared on the knuckles, elbows and lateral aspects of the thighs. The patient had a pilonidal sinus, which became infected; it was operated on three months ago. The patient lost 40 pounds (18 Kg.) in the last year, since the onset of the illness.

There are generalized tenderness of the muscles and pronounced atrophy of the muscles of the upper part of the back and of the shoulders. There is edema of the lower lids and seborrhea about the nasal folds and ears. On the shoulders, elbows, knees and knuckles are patches of dusky erythema, which are most conspicuous on the elbows; the dusky areas are slightly scaly and lichenified. There is slight edema of the fingers. There is pain on movement of all joints, with resulting limitation of motion. On the lateral aspect of the upper part of the thighs there are two ill defined areas of pigmentation, depigmentation, telangiectasia and atrophy. General physical examination revealed no essential abnormalities except for a roughened first mitral sound. The systolic blood pressure was 110 and the diastolic 70.

Histologic examination of a specimen of skin and of a specimen taken from the apparently unaffected pectoral muscle showed a normal epidermis, slightly perivascular infiltrations of small round cells and large mononuclear cells in the corium and in the subcutaneous tissue. There was a slight increase in loose perivascular connective tissues. A few small arteries showed thickened walls. A small fragment of striated muscle appeared normal. There was no evidence of trichinosis.

Roentgenograms showed slight hypertrophic changes of the bones of the elbows and slight hypertrophic changes of the bones of the right hand forming the distal interphalangeal joint of the fifth digit.

Examination of the blood showed 86 per cent hemoglobin, 4,420,000 red blood cells, with no basic stippling, and 9,800 white blood cells, with 53 per cent segmented polymorphonuclear leukocytes, 9 per cent stab cells, 26 per cent lymphocytes, 4 per cent monocytes, 7 per cent eosinophils and 1 per cent juvenile cells. Chemical examination of the blood disclosed a normal content of sugar and urea and 1.3 mg. of creatinine per hundred cubic centimeters. The Wassermann and Kahn reactions were negative. The basal metabolic rate was within normal limits. Examination of the urine showed lead within normal limits, 1.64 Gm. of creatine and creatinine and occasional red blood cells. Aerobic and anaerobic cultures of muscle were sterile.

The patient was treated with alpha tocopherol (vitamin E), 2.2 cc. intramuscularly twice weekly for four weeks, and with vitamins A and D, 1 capsule three times a day. Decided amelioration of all symptoms was noted, and the patient was discharged with the condition much improved on Feb. 2, 1941.

DISCUSSION

DR. PAUL GROSS: I agree with the diagnosis of dermatomyositis and am gratified to see the response to alpha tocopherol. Recent investgation carried out at the Cornell Medical Center has shown that dermatomyositis responds to whole wheat germ. In an attempt to corroborate these results, I administered intramuscular injections of calcium pantothenate in a case of dermatomyositis. Neither the clinical picture nor the creatine excretion were influenced by this therapy. On the basis of the experimental work on vitamin E, alpha tocopherol is the logical treatment for dermatomyositis, and this makes the therapeutic result in this patient particularly valuable.

DR. ARTHUR SAYER: It is important to differentiate poikilodermatomyositis and dermatomyositis. Petges and Clejat originally described a case of poikilodermatomyositis associated with muscular sclerosis. The patient presented gives a characteristic history of onset with a sore throat, followed by muscular tenderness and weakness. This sequence is typical in dermatomyositis. The cutaneous changes occurring in dermatomyositis are secondary, and I do not think that they are significant. O'Leary and Waisman recently reported (ARCH. DERMAT. & SYPH. **41**:1001 [June] 1940) a series of cases of dermatomyositis studied at the Mayo Clinic and emphasized the inflammatory and degenerative changes in the muscles. It may be mentioned that in some cases of dermatomyositis the condition is rapidly progressive and may end in death, while in others it is slow and benign. The condition in this case belongs in the latter category.

DR. RUDOLPH L. BAER (by invitation): The improvement in this case may be due just to spontaneous remission. However, all who have observed the case, as well as the patient himself, had the impression that improvement followed treatment with injections of alpha tocopherol. I shall follow the suggestion to make further creatine studies and shall also continue with the injections of alpha tocopherol.

Epidermodysplasia Verruciformis (Lewandowsky and Lutz). Presented by DR. HENRY SILVER.

Miss H. M., aged 26, is a deaf-mute. The condition followed an automobile accident at the age of 2 years. About fifteen years ago warty growths began to develop. In the course of years they involved the fingers, palms, knees and legs. The lesions were electrodesiccated from time to time, but some recurred and others left keloidal scars. About twelve years ago there appeared a diffuse acneform eruption of the face. Two sisters had common warts on the hands early in life, which disappeared spontaneously within a few years. The parents and siblings are alive and well. There is no tuberculosis or cancer in the family.

The face is erythematous, and there are many pustules and comedos interspersed with areas of telangiectasia. Brownish seborrheic keratoses are distributed over the face and forehead; they are particularly numerous on the temples. There are large confluent translucent warty lesions involving the entire back of the index finger, the thumb and the distal phalanges of the ring finger of the right hand. On the back of the hand are scattered hypertrophic scars. The thumb, index finger and little finger of the left hand are similarly involved. On the left forearm there are lesions the size of a pea. A large raised verrucous plaque covers the major portion of the right palm. There is clubbing of the fingers. The nails show no changes. On the knees, legs and toes are isolated scattered verrucous lesions the size of a pea or of a hazelnut.

Several lesions from the fingers and face removed for histologic study showed typical verruca vulgaris. A section from a lesion clinically diagnosed as seborrheic keratosis showed a decided downgrowth of the epidermis with the formation of horn whorls. This ectodermal hyperplasia indicates beginning carcinomatous change.

Intradermal tuberculin tests with dilutions up to 1:1,000 gave negative results. Roentgenograms of the chest showed no abnormalities. Examination of the urine for bromides and iodides gave negative results. Investigations for filtrable virus made by Dr. Shwartzmann gave negative results.

DISCUSSION

DR. LOUIS CHARGIN: It is difficult to establish a definite diagnosis in this case. In the first place, in Lewandowsky-Lutz disease one does not, as a rule, find lesions on the palms. In this case the lesions on the palms are extensive and well developed. Secondly, while there is a history of warts in the siblings, the lesions are said to have spontaneously disappeared; if the sisters had the same disease, since the condition is familial, that fact should speak against the diagnosis. One point in favor of the diagnosis as presented are lesions which resemble seborrheic warts, since such lesions are associated with the disease. With respect to other lesions, I can see that they may be common warts. The vacuoles observed histologically in this disease are also found in many other diseases, even in common warts. In view of this I do not believe one can suggest the diagnosis presented on the basis of the histologic structure alone. The fact that the condition in this case began later in life is not in favor of epidermodysplasia. There are many points in favor of the diagnosis presented and equally many against it.

DR. CHARLES WOLF: This case is rather puzzling. Many authors consider this condition to be a type of generalized verruca vulgaris. Some of the lesions undergo malignant degeneration. The disease occurs frequently in Orientals. In 40 per cent of the reported cases the patients have been Japanese. In this country the disease is infrequent. The clinical appearance of these lesions shows a characteristic translucency not seen in common warts. Gans, Hoffmann and Kogoj do not think that this condition is a distinct clinical entity. In my opinion the case presented is one of epidermodysplasia verruciformis.

DR. SAMUEL M. PECK: It is fortunate that two biopsy specimens were taken. The first specimen showed the picture of verruca vulgaris; the one from the face showed formation of horny whorls and a tendency toward downgrowth of the epidermis. In spite of the history and considering the picture as a whole, I think it is justifiable to make a diagnosis of epidermodysplasia verruciformis.

DR. HENRY SILVER: Since Lewandowsky and Lutz described the disease only 28 cases resembling the original have been recorded. Half of the number appeared to be cases of extensive verruca vulgaris or verruca plana. The condition in the case presented resembles the disease described by Hopf as acrokeratosis verruciformis, in which the lesions are confined to the hands and feet and appear in the form of massive warty formations.

I cannot agree with one point raised by Dr. Chargin, although his analysis of the case is accurate. He considered the fact that the disease appeared late in life as a point against the diagnosis. Epidermodysplasia belongs to the group of genodermatoses, and it may appear shortly after birth or before puberty.

Epitheliomas of the forehead and temples are commonly encountered; this led some observers to regard the disease as a precancerosis. Dr. Chargin seemed to agree with Kogoj that the vacuolating degeneration is common to many keratotic anomalies. I agree with Dr. Wolf that epidermodysplasia verruciformis is a variety of Hoffmann's verrucosis generalisata.

Palmar and Plantar Keratosis, Improved by Parenteral Liver Therapy.
Presented by DR. PAUL GROSS.

B. A., a housewife aged 32, was seen at the Hospital for Joint Diseases in February 1939. She had an eruption on the palms and soles and had been receiving antisyphilitic treatment since February 1936.

Both palms showed a diffuse keratosis of considerable thickness. The soles were covered with thick scaly keratosis, especially over the pressure areas. On

the elbows were ill defined scaly patches with small follicular papules. The patient had lost 5 pounds (2.3 Kg.) within three weeks. She suffered from constipation.

She received two injections of sodium thiosulfate, sixteen injections of liver extract and cod liver oil by mouth. The antisyphilitic therapy, consisting of injections of bismuth subsalicylate, was discontinued. By June 1939 the condition had improved and the patient was in better health. For several months the effect of nicotinic acid and riboflavin on the eruption was studied, but there was no improvement. In November 1940, after an induced abortion, the patient returned to the clinic complaining of weakness and nervousness. The keratosis of the palms and soles was as pronounced as in 1939.

The patient was given injections of 2 cc. of concentrated liver extract. After twenty-eight injections the keratosis of the palms disappeared and that of the soles cleared except for a narrow zone at the edge of the heels.

The Kahn and Kline reactions were negative.

DISCUSSION

DR. SAMUEL M. PECK: The crude liver extract which Dr. Hopkins and Dr. Gross originally used in exfoliative eruptions can no longer be obtained. Is Dr. Gross using another form of liver? The extract that I now employ does not give the same results that I originally obtained with the crude extract.

DR. CHARLES WOLF: It is not clear to me whether this case is one of vitamin deficiency or of an arsenical keratosis. Can the result obtained be attributed to vitamin B therapy, vitamin B being the active vitamin in liver extract, or is it due to the excretion of arsenic over a period of time? I believe the condition is a keratosis of syphilitic or arsenical origin.

DR. GIRSCH D. ASTRACHAN: In reference to the crude liver extract, which Dr. Peck stated is difficult to obtain, I wish to state that I have been using this type of liver extract for the past five years and I am still using it. The extract contains approximately 1 U. S. P. injectable unit per cubic centimeter. I prefer the crude preparations because they contain the necessary detoxifying materials, while the purified and concentrated extract contains little or none of these important ingredients. As to the possible explanation of the beneficial effect of liver extract in some cases, Dr. MacKee and I tried to answer this question in reference to patients intolerant to arsenicals, heavy metals and radiation (MacKee, G. M., and Astrachan, G. D.: *J. Invest. Dermat.* **3**:409, 1940). In many of the cases studied the injection of liver extract was followed by improvement in the blood count as well as in hepatic function (decrease in the icterus index).

DR. PAUL GROSS: I agree with Dr. Peck that the crude liver extract of a few years ago was more effective than the present concentrates. Further investigation is necessary to decide which factor of the vitamin B complex is important for certain dermatoses. I believe that the synergistic action of the natural vitamin B complex cannot be duplicated as yet by synthetic products. In answer to Dr. Wolf, the patient had antisyphilitic treatment, but the palmar and plantar keratosis did not resemble arsenical or syphilitic keratosis. The condition of the scalp was alopecia areata, and the patient also had lesions on the elbows resembling those seen in pellagra. It is possible that the hepatic damage caused by a syphilitic infection and by arsenicals was in part responsible for the development of a vitamin deficiency.

Pityriasis Rubra Pilaris. Presented by DR. SAMUEL M. PECK and DR. LOUIS CHARGIN.

A woman aged 56 was treated for syphilis at the clinic of Mount Sinai Hospital from January 1932 to January 1934. On Nov. 7, 1940 she presented an eruption which had been present for three weeks. It consisted of large and small patches of scaling and redness and was situated on the abdomen and arms, in the axillas

and behind the ears. The eruption rapidly became disseminated. The initial lesions consisted of follicular papules which became confluent. The eruption rapidly assumed the character of pityriasis rubra pilaris with typical lesions on the hands, especially the fingers.

Two biopsy specimens were taken. The sections showed hyperkeratosis and follicular keratotic plugs. In some areas the epidermis was thin and in others acanthotic. There were scattered areas of intercellular edema among the basal cells. Below the epidermis there were many dilated blood vessels with some perivascular infiltration. The elastic tissue was fragmented and absent in many areas. The collagen fibers also were involved. The histologic diagnosis was pityriasis rubra pilaris.

Vitamin A studies in December 1940 showed 81 U. S. P. units of vitamin A and 240 mg. of carotene per hundred cubic centimeters of blood serum and on Jan. 7, 1941 65 U. S. P. units of vitamin A and 200 mg. of carotene. After the ingestion of 200,000 U. S. P. units of vitamin A per day, the examination of the blood serum on February 21 showed 120 U. S. P. units of vitamin A and 260 mg. of carotene per hundred cubic centimeters.

Vitamin A in doses of 200,000 U. S. P. units a day by mouth was begun early in January. On January 11 there was a definite flattening of the papules. The skin gave the appearance of generalized erythroderma, and no individual papules could be made out. There was continuous improvement, and on January 25 the dose was increased to 300,000 U. S. P. units per day, followed by definite involution of the cutaneous eruption.

DISCUSSION

Dr. Samuel M. Peck: Dr. Gross has presented a patient with pityriasis rubra pilaris showing a striking result following the use of vitamin B (Arch. Dermat. & Syph. **43**:751 [April] 1941; **44**:270 [Aug.] 1941). From the discussion it appeared that the underlying process was a vitamin B deficiency. In a paper from the Mayo Clinic Brunsting and Sheard (Arch. Dermat. & Syph. **43**:42 [Jan.] 1941) apparently proved that pityriasis rubra pilaris is essentially a vitamin A deficiency. Our patient also presented a classic example of pityriasis rubra pilaris both clinically and histologically.

The vitamin A concentration in the blood was at a low normal level. The ingestion of 200,000 U. S. P. units of vitamin A per day has resulted in a remarkable involution of the eruption. The patient shows an erythroderma with some exfoliation. It may be, as Dr. Gross has suggested, that as much as possible has been achieved with vitamin A and this substance will have to be supplemented by vitamin B to obtain complete involution. In the light of Dr. Gross's results, the disease is possibly due to the combined deficiencies of vitamins A and B.

Dr. Paul Gross: This patient was treated in the early stages of an acute eruption and therefore responded promptly to vitamin A therapy. The residual erythroderma would be an indication for further therapy with vitamin A as well as with vitamin B complex. The fact that pityriasis rubra pilaris responds to vitamin A and to parenteral liver therapy is by no means paradoxic, and a discussion of the subject can be found in my paper on vitamin B complex (Arch. Dermat. & Syph. **43**:504 [March] 1941).

Dr. Louis Chargin: This case differs from the usual case of this condition in that the eruption ran an acute course with rather rapid development. The characteristic features include the seborrhea-like eruption on the face and scalp and infiltration on the arms and back. It is remarkable to observe the striking improvement following the vitamin therapy, in comparison with the results seen in former days. One must bear in mind, however, that the eruption, especially in young persons, disappears without any treatment and in a short time, so that it is difficult to attribute this improvement definitely to the use of vitamin A. Until this course is consistently reproduced in a number of cases, one must be cautious in evaluating the results obtained.

Lichen Sclerosus et Atrophicus (Hallopeau). Presented by DR. DAVID BLOOM.

E. B., a woman aged 43, of white and Indian stock, came to the clinic of the Sydenham Hospital presenting an eruption which began twenty-five years ago. The patient is in good health except for having the eruption, which involves the upper part of the back and chest, the right breast, the flexor surfaces of the wrists, the genitoanal region and the right instep.

Clinically, four types of lesions can be differentiated. On the upper part of the back there are two somewhat elevated white plaques, one the size of a silver dollar and the other somewhat larger than a nickel, formed apparently by coalescence of numerous papules. In the center of the plaques there are blackish, horny follicular plugs, which give the palpating finger a sensation of roughness. A similar lesion is present on the flexor surfaces of the wrists and is arranged in linear configuration. The duration of these lesions is from ten to fifteen years. Another type of lesion is seen on the right breast just beneath the areola and presents a flat plaque the size of half a silver dollar. It consists of round white somewhat infiltrated flat lesions the size of a pea, which have coalesced to form the patch. This plaque is smooth and does not show any keratotic follicular plugs. The duration of this lesion is about three months. The third type of lesion is located on the upper part of the back somewhat to the left of the other two rough plaques; it is a roundish area 2½ inches (6.5 cm.) in diameter, flat and not infiltrated and consists of numerous depigmented round macules, the size of a pea, which give the impression of being depressed slightly below the skin. A similar lesion of about the same size is situated over the manubrium sterni, and a plaque the size of a palm extends symmetrically from below the vulva toward the posterior aspect of the anus. The duration of these lesions is about twenty-five years. On the inner aspect of the right heel there is one erythematous rough scaly slightly elevated papule the size of a pea, and an erythematous rough scaly slightly elevated linear lesion 1 inch (2.5 cm.) long. These lesions appeared several months previously.

Only the rough lesions on the upper part of the back and on the wrists and the right heel produce a moderately severe pruritus, while no subjective symptoms are associated with the other two types of lesions.

The past history of the patient has been normal, except that she had a hysterectomy and salpingectomy two years ago.

Laboratory examinations, which included the Wassermann test, examination of the urine and a complete blood count, gave negative results.

Histologic examination of the sections taken from the elevated rough plaque on the back and from the lesion on the right breast confirmed the diagnosis of lichen sclerosus et atrophicus.

DISCUSSION

DR. WILBERT SACHS: The histologic sections are typical for lichen sclerosus et atrophicus (Hallopeau). I do not believe the condition is a variety of scleroderma. There is a peculiar change in Hallopeau's disease directly underneath the epidermis which is not found in any other dermatosis.

DR. DAVID BLOOM: Opinions on this problem should be based on observation of many cases. Montgomery (ARCH. DERMAT. & SYPH. **42**:776 [Nov.] 1940) has concluded on the basis of 46 cases that lichen sclerosus et atrophicus should be distinguished from morphea guttata and from lichen planus atrophicus. I agree with this opinion. In my case the combination of the various types of lesions is of interest.

Urticaria Pigmentosa Acquisita. Presented by DR. MAX BERKOVSKY.

A married man aged 36, an automobile salesman, noticed the first lesions about seven years ago. There are no concomitant subjective symptoms. During the last year many new lesions have appeared.

The patient presents numerous hemorrhagic discrete macules, varying in size from that of a pinpoint to that of a small pea and distributed over the trunk and extremities, with a few scattered on the face. The lesions are nonpruriginous but urticate on rubbing.

The Wassermann reaction was negative, and the blood count and the urine were normal.

Histologic examination by Dr. Peck showed the characteristic picture of urticaria pigmentosa.

Lichen Planus Appearing During Antisyphilitic Treatment. Presented by Dr. William Leifer.

S. H., a Negress aged 28, a domestic, was admitted to the Central Social Hygiene Clinic of the Department of Health on July 2, 1940, with a diagnosis of late latent syphilis. The Wassermann reaction on two occasions was 4 plus. Examination of the spinal fluid showed no abnormality. A complete physical examination showed no abnormalities, and there was no evidence of cutaneous lesions.

The patient was treated regularly from July 2 until Feb. 27, 1941 by the continuous alternating method. By Feb. 14, 1941 she had received a total of sixteen injections of bismuth subsalicylate and fourteen injections of neoarsphenamine (0.45 Gm.). On February 14 she complained of an itching eruption which had first appeared some four days before. Despite the presence of the eruption she was given another dose of neoarsphenamine, which did not provoke any exacerbation of the eruption. The eruption first appeared on the neck and on the upper part of the trunk but later spread to involve the face and upper extremities.

The lesions are scattered diffusely over the anterior and posterior part of the chest, the flexor surfaces of the elbows, the chin, the nasolabial folds and the lower eyelids. On the trunk and neck many lesions are distinctly follicular, appearing as rough spiny papules. There are also present here, and in the other areas mentioned, raised flat shiny roughly polygonal papules. The lesions on the chin, and in the nasolabial folds particularly, are confluent and almost black. There are some white reticulated patches on the buccal mucosa, bilaterally, opposite the molar teeth, and there are a few smooth whitish patches on the dorsum of the tongue.

DISCUSSION

Dr. Louis Chargin: I agree that the eruption represents a form of arsenical dermatitis.

Dr. Paul Gross: I suggest that the patient be treated with injections of liver extract and nicotinic acid by mouth.

Dr. Charles Wolf: I have treated about 15 patients with lichen planus with intramuscular injections of liver extract and have given each patient about twenty injections. I have failed, however, to obtain beneficial results.

Dr. William Leifer: The condition is clinically lichen planus. The question is whether it is a lichenoid arsenical eruption or lichen planus occurring in the course of arsenotherapy.

Ulcer of the Leg in a Patient with Sickle Cell Anemia. Presented by Dr. Louis Chargin.

A Negress aged 24 is a patient at Mount Sinai Hospital. Five years ago a small ulcer appeared on the tibial aspect of the right leg. This ulcer has enlarged to its present size of 2 inches (5 cm.) in diameter. It is deeply excavated, with a perpendicular wall and a rough grayish base. Two years ago another ulcerative process began in the right genitocrural region. This was diagnosed as granuloma inguinale and has responded well to injections of antimony and potassium tartrate.

Examination of the blood showed 45 per cent hemoglobin, 2,520,000 red blood cells, 10,100 white blood cells, with 48 per cent segmented polymorphonuclear leukocytes, 4 per cent nonsegmented polymorphonuclear leukocytes, 3 per cent eosinophils, 1 per cent basophils, 38 per cent lymphocytes and 6 per cent monocytes, and 300,000 platelets. A good proportion of the red cells showed the characteristic sickle shape. The icterus index was 10 (acetone method).

Acnitis (Acne Agminata-Crocker). Presented by DR. ARTHUR SAYER.

R. K., a white man aged 35, married, a former professional soccer player, came to the United States from Austria about one year ago. He has been treated at Mount Sinai Hospital for a duodenal ulcer as well as for the present eruption.

The patient presents a papular eruption on the cheeks, and to a much lesser extent on the chin and anterior part of the chest. The lesions are the size of a split pea and the color of ham; there is no evidence of pus in them. The eruption first appeared about ten months ago, and since then new lesions have appeared slowly and have persisted. On each cheek there are about two dozen discrete papules showing no tendency toward grouping. The lesions on the chin and on the chest are fewer and are the size of a pinhead. There are no subjective symptoms.

The patient had active pulmonary tuberculosis in 1931 and had an artificial right-sided pneumothorax from 1931 to 1937. At present the condition is not active, and he has no pulmonary symptoms.

Roentgenograms of the chest in October 1940 showed the heart and trachea displaced somewhat to the right, with evidence of considerable thickening of the pleura on the right side. There were calcification and fibrosis of the upper lobe of the right lung. There was no evidence of recent pulmonary disease. The lumbar spines showed moderate scoliosis, with the convexity toward the right. Intravenous pyelograms showed that the upper part of the urinary tract on the left side was normal but the urinary tract on the right side showed slight dilatation with an angulation of the ureter at the ureteropelvic junction. Both ureters appeared normal. The psoas margins were distinct. Urinalysis showed a specific gravity of 1.032, occasional red blood cells and rare white blood cells, The Wassermann reaction was negative.

DISCUSSION

DR. WILLIAM LEIFER: I have used tuberculin therapeutically in cases of papulonecrotic tuberculid and suggest that it be used with extreme caution. I see no objection to trying gold sodium thiosulfate in small doses.

DR. ERNST W NATHAN (by invitation): I have given some patients with acnitis tuberculin in small and gradually increasing doses with satisfactory results. In some cases I combined tuberculin and a gold compound with good results.

DR. ARTHUR SAYER: It is interesting to note that in most of the cases of acnitis reported by Maloney (ARCH. DERMAT. & SYPH. **15**:285 [March] 1927) there was a negative reaction to tuberculin. I shall follow the suggestion with regard to therapy.

Pyoderma Chancriforme Faciei. Presented by DR. MARION B. SULZBERGER.

Mrs. F. H., aged 31, noticed a lesion below the left eye about Feb. 6, 1941. The lesion increased to the size of a pea and several days after its onset began to form a central crust. On February 13 a swelling of the gland at the angle of the jaw was noticed.

On the inner malar region there is an erythematous indurated lesion the size of a pea with a brownish flat central adherent crust. The center is almost concave. At the angle of the left jaw there is a freely movable nontender gland the size of a bean.

The lesion healed quickly under wet dressings of a saline solution and an ointment of 3 per cent ammoniated mercury. Repeated dark field examinations, as well as the Wassermann test, gave negative results. The culture revealed a hemolytic staphylococcus and a streptococcus.

DISCUSSION

DR. RUDOLPH L. BAER (by invitation): This type of lesion differs from granuloma pyogenicum in that it is indurated and not accompanied by bleeding on removal of the crust. On the contrary, when the crust is removed the amount of serum that can be expressed resembles the rather profuse serous flow that one gets on examining a primary syphilitic lesion. Erich Hoffmann first described this condition (*Arch. f. Dermat. u. Syph.* **170**:403, 1934).

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

GEORGE C. ANDREWS, M.D., *Chairman*

HERMAN SHARLIT, M.D., *Secretary*

Feb. 4, 1941

Chancroid; Lymphogranuloma Venereum (Healed); Syphilis. Presented by BORRIS A. KORNBLITH, M.D.

A. S., a 40 year old Negro, appeared at the Central Social Hygiene Clinic of the Department of Health on Jan. 24, 1941 because of two large ulcerations on his glans penis of six weeks' duration. Nine months before the onset of these lesions the patient had had a penile chancre the size of a pinhead. This healed after three intravenous injections of neoarsphenamine and one intramuscular injection of a bismuth compound. An abscess in the right inguinal region was incised and drained six months ago.

There are two ragged deep ulcerations, 15 mm. in diameter, on the dorsum of the glans penis. These are covered by a dirty shaggy exudate. A healed scar of a previous incision and drainage is present in the right groin. There is no inguinal adenopathy at present.

The Kahn reaction was 4 plus. The Frei test and the Ducrey vaccine cutaneous test elicited positive reactions. Dark field examinations gave negative results. Smears (methyl green pyronine stain) showed Ducrey organisms.

During the past nine days the patient has been taking sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole), 0.5 Gm. four times a day. The lesions are healing.

This case illustrates the presence of three venereal diseases simultaneously in the same patient.

DISCUSSION

DR. GEORGE C. ANDREWS: The condition has responded to sulfathiazole in small doses, and there is no incompatibility between this drug and bismuth and arsphenamine, showing that they can all be used for a patient at the same time.

DR. E. WILLIAM ABRAMOWITZ: When sulfanilamide and its derivatives were first introduced, the question arose as to whether it would be safe to use those drugs at the same time as arsphenamine should the occasion arise. Dr. Downing, of Boston, told me that it was common practice to use sulfanilamide for gonorrhea and arsphenamine for syphilis for a patient concurrently and that he had never seen any untoward reaction.

In connection with the use of sulfathiazole, I should like to know whether Dr. Kornblith has encountered any side effects, not only on the skin but more

serious reactions such as anuria or hematuria. I wonder if those complications occur with the smaller doses such as Dr. Kornblith uses. I think it would be a good idea when the patient presents only ulcerations to cover the lesions with sulfanilamide ointment instead of giving the drug by mouth. I wonder if the same result could not be accomplished in this manner.

DR. BORRIS A. KORNBLITH: Thus far 200 patients with chancroid have been treated at this clinic. I had the privilege of reporting before this society about three years ago on the first 25 cases in which sulfanilamide was used (ARCH. DERMAT. & SYPH. **38**:476 [Sept.] 1938), in all of which the treatment was successful. At this time there are 175 additional cases, in 150 of which sulfanilamide was given and in 25 sulfathiazole. In all a cure has been effected. There has not been a single case thus far, when the diagnosis was certain, in which the condition was resistant.

In reference to the comparative efficacy of sulfanilamide and sulfathiazole, I believe that sulfathiazole is as good as sulfanilamide, and perhaps better, since a smaller amount is used, a shorter time is necessary and there is complete success. All patients were ambulatory, and no untoward after-effects were observed. I realize that anuria and hematuria may occur. Negroes tolerate this drug rather better than white persons, and since the major portion of patients in our clinic is Negro, this may account for the absence of complications. In all only 70 patients have been treated with sulfathiazole. The oral dose of sulfathiazole, 2 Gm. daily for a ten day period, seems more suitable in the treatment of chancroid.

In regard to the use of the powdered sulfanilamide locally, it does not prove so effective, for deep-seated ulcerations in particular or for lesions of long duration. It has, however, proved effective in the treatment of small, superficial ulcerations. It may be true that small ulcerations would have healed spontaneously or with any form of therapy.

The finding of the Ducrey bacillus is to my mind the most important factor in the diagnosis of chancroid, and the use of the methyl green pyronine stain is the most effective way of demonstrating it. Whenever the organism can be demonstrated the drug under discussion produces a cure.

Chancroid. Presented by DR. BORRIS A. KORNBLITH.

H. L., a 58 year old Negro, appeared at the Central Social Hygiene Clinic of the Department of Health on Jan. 15, 1941 because of an extensive ulceration about the corona and swelling of the prepuce of two months' duration. There was no history of syphilis or of recent gonorrhea.

On examination a large serpiginous ulceration, measuring 4 by 3 cm., was seen encircling the corona. The surface appeared dirty and was covered by a slough. There were, in addition, a severe paraphymosis and bilateral shotty lymphadenopathy. Dark field examination gave negative results. Smears and methyl green pyronine stain showed Ducrey organisms, and a Ducrey vaccine cutaneous test gave a positive reaction.

The patient was given powdered sulfathiazole and advised to cleanse the ulcer with soap and water and apply the powder locally twice daily. This was continued for nine days. The lesion looked somewhat cleaner but showed no evidence of healing. A smear for Ducrey organisms proved negative. On the tenth day the administration of sulfathiazole by mouth, 0.5 Gm. four times a day, was begun. After nine days of this therapy the ulcer is about half its original size and is healing rapidly. The patient is still under treatment.

He gave a negative reaction to a Frei test on his left forearm and a positive reaction to a Ducrey vaccine test on his right forearm.

The case is presented to show the relatively greater efficacy of sulfathiazole given by mouth for systemic action than as a powder applied locally. For small, superficial chancroids the powder has been sufficient to produce healing. The more extensive chancroids do better with oral use of the drug.

DISCUSSION

DR. HERMAN SHARLIT: Is sulfathiazole more effective than sulfanilamide, or are both effective?

DR. BORRIS A. KORNBLITH: Since sulfanilamide apparently has proved itself to be 100 per cent successful thus far in this group of cases, it is hard to present a comparison. Nevertheless, I believe that sulfathiazole may be considered better, in that a smaller dose is used effectively over a shorter period and the toxic reactions are certainly less. There is no nausea, vomiting or cyanosis, and so far no other bad effect. Therefore, if 25 cases are taken as a criterion, the drug may be considered better for this purpose than sulfanilamide. Time will tell.

DR. GEORGE C. ANDREWS: In your comparison of the two drugs, what dosage of sulfanilamide was used?

DR. BORRIS A. KORNBLITH: Sulfathiazole is given for ten days in divided doses: 0.5 Gm. four times daily. Then administration of the drug is stopped whether or not the lesion is healed, as it will heal without further therapy. On the other hand, the dosage of sulfanilamide is 1.2 Gm. four times a day for five days, followed by 0.6 Gm. four times a day for an additional nine days. Thus, this drug is administered for fourteen days.

Lymphogranuloma Venereum. Presented by DR. BORRIS A. KORNBLITH.

R. W., a 29 year old Negro, appeared in the Central Social Hygiene Clinic of the Department of Health on Jan. 20, 1941 with a painful swelling, the size of an orange, in his right groin, of three weeks' duration. He had been treated in 1939 for a chancroidal infection, which healed completely after seven days' treatment with sulfanilamide. About three weeks before admission he observed a pinhead-sized ulceration on the corona. This healed spontaneously in about ten days. He observed the inguinal swelling about the same time.

The patient shows a recently healed 4 mm. nodule on the corona and a purple nonfluctuant bubo, 10 cm. in diameter, in the right inguinal region.

The Wassermann reaction of the blood was negative. Two dark field examinations and smears for Ducrey organisms gave negative results. The Frei test and the Ducrey vaccine cutaneous test both gave positive reactions.

The patient was given sulfathiazole, 0.5 Gm. four times a day, for two weeks. The swelling promptly subsided.

DISCUSSION

DR. EUGENE TRAUGOTT BERNSTEIN: At present I have a patient, a Negress, with extensive lymphogranuloma venereum, who has been seen by Dr. Kornblith. I gave her sulfathiazole, and she did not respond; she responded much better to sulfanilamide. In regard to diagnosis, a mistake is often made in evaluating the reaction to a Frei test, which is positive, I think, only after the infection has been present about six weeks or two months. I want to ask Dr. Kornblith if he has had that experience. After the reaction to one Frei test is positive, a second always elicits a positive reaction, because the first is apt to sensitize the patient.

DR. BORRIS A. KORNBLITH: On a number of occasions I have repeatedly tested the same patient who did not have lymphogranuloma venereum, and I have obtained persistently negative results. This proved that the patient had not become sensitized to the Frei antigen. Once negative, so far as I know, the reaction does not become positive (in the absence of infection). The reverse, however, may be true occasionally. The reaction to a Frei test performed repeatedly on a limited area of skin may become negative. However, another test made concurrently on another portion of the skin will give a positive reaction. Of late there have been reports in the literature that after thorough treatment with sulfanilamide, one observer has been able to reverse the Frei reaction from positive to negative. I have tried to confirm this observation but have been unsuccessful so far. The Frei reaction, once positive, has remained positive in spite of any form of therapy. From that

point of view, the evaluation of the result of a Frei test can be confusing in a patient applying for treatment of some other disease.

DR. HELEN CURTH (by invitation): I have had the same experiences with the Frei test. I have had only occasional false positive reactions in cases of diabetes; the reaction to a Frei test has been positive although the patient has never had lymphogranuloma venereum. I tried control tests with saline solution, and the reactions were also positive. This is not true in all cases of diabetes, however. With regard to treatment, I have tried sulfanilamide and sulfathiazole as salves, although, I am sorry to say, only in cases of superficial chancroid. This method has worked well, and generalized toxic reactions have been avoided.

DR. FRED WISE: Has Dr. Kornblith had any experience with patients with established lymphogranuloma venereum who give repeatedly negative reactions to the Frei test, said to be due to an anergic state?

DR. THEODORE ROSENTHAL: Last week I talked with an investigator who was himself infected experimentally with lymphogranuloma venereum. He had rather a stormy febrile course for eight to ten weeks, during which the reaction to a Frei test was positive. Sulfathiazole treatment was instituted, and now, six or seven months after the initial infection, the Frei reaction has become negative.

DR. CHARLES WOLF: I have heard a great deal about the therapeutic value of sulfathiazole in external lesions. It would be interesting to know what effect sulfathiazole or sulfanilamide and its other derivatives have on other manifestations of the disease, such as stricture of the rectum and glands in the ileac region of the pelvis. Another thing comes to mind: I have heard that the Frei reaction remains positive. When patients drift from one clinic to another, how is one going to know whether a positive Frei reaction is caused by the particular manifestations of the condition the patient has on a second investigation or whether it is a hangover from the first infection? Other things being normal, one must consider new manifestations as being suggestive of lymphogranuloma venereum.

DR. E. WILLIAM ABRAMOWITZ: If the patient is taking bromides or iodides, might he not show a false positive reaction to a Frei test? It is known that the primary lesion of lymphogranuloma venereum is sometimes so inconspicuous that it is not seen and that the lesion heals rapidly when it is seen. In other words, this disease tends toward spontaneous healing and later progression. I was wondering what the evolution of the disease is going to be under treatment with sulfanilamide and its derivatives, whether one is just clearing up the visible manifestations and whether one will be able to control the late and more serious manifestations, such as rectal stricture. I do not know how long cases have been observed by Dr. Kornblith, but has he any observations as to what might happen to patients later on? The literature is of course recent. I am reminded of the old treatment of syphilis: mercury healed the chancre and subsequent symptoms but did not prevent the later sequelae.

DR. MAURICE J. COSTELLO: My experience at Bellevue Hospital, where a fair number of patients with lymphogranuloma venereum are treated, tallies well with that of Dr. Kornblith, especially in the results of oral administration of sulfanilamide. I can cite an experience similar to that of Dr. Curth. I observed in the dermatologic ward at Bellevue Hospital a patient with xanthoma diabeticorum in whom the reaction to an intradermal test with Frei antigen was positive when he had an elevated blood sugar level and later negative when there was a reduction in the blood sugar to normal. I should like to ask Dr. Kornblith what experience he has had with chick embryo Frei antigen.

DR. NATHAN SOBEL: I have observed several cases of acute lymphogranuloma venereum in which there was a positive Wassermann reaction at the onset of the disease. This turned out to be a false positive reaction which became negative within four to six weeks without the patient's receiving antisyphilitic therapy. The positive Wassermann reaction did not recur even when the patient was followed for several years.

DR. BORRIS A. KORNBLITH: The Frei test is not 100 per cent specific. Some of the French observers found the test to be exact in something like 97 per cent of the cases, leaving 3 per cent in which false positive reactions were obtained.

How many cases are there of lymphogranuloma venereum with negative reactions to Frei tests? I had occasion to present 2 such cases to Dr. Frei when he was visiting here. Among 750 cases there were 4 which were undoubtedly of lymphogranuloma venereum from the clinical point of view, and in these 4 the condition was anergic. Apropos of this, it was found that in at least 20 per cent of a series of 220 cases there was no febrile reaction, chills or headache after the initial 0.3 cc. of Frei antigen was given intravenously, in spite of the fact that the reaction to a Frei test was positive. What form of anergy exists in such cases is a subject which demands further study.

As to the effect chemotherapy has on stricture of the rectum, I think it is too soon to evaluate sulfathiazole. However, sulfanilamide does affect acute proctitis and secondary infections of the rectum. In my experience I found that sulfanilamide works just so far and then stops; if its administration is combined with the intravenous administration of antigen, stricture of the rectum is finally produced, which represents the healed and not the active stage of the disease. It must be remembered that some patients seen now with stricture of the rectum and fibrosis present healed conditions for which nothing was done; they hardly realized they had the disease. The effectiveness of sulfanilamide and sulfathiazole in reducing secondary manifestations and future destructive effects is something to be judged as time goes on. Patients followed since 1931 and 1932 have shown no further progression of disease once treatment was initiated. I have good reason to feel confident that the more serious secondary phases are not likely to develop.

It would be well to subtract 30 per cent from the good results I have enumerated, because in 30 per cent of one series the condition healed spontaneously no matter what was done, although it did take a little longer. Even with the 30 per cent subtracted, there is still a high percentage of clinical cures with sulfathiazole.

Concerning the development of a positive reaction to a Frei test in patients who are taking other drugs, such as bromides and iodides, I have encountered no cases of this kind; but since a thorough history of associated drug therapy is not obtained in the clinic, there is at this time no satisfactory answer to this question.

I apologize for not answering the question about the chick embryo antigen. Work is being done on this now, and I am not at all sure how good or bad the substance will prove to be. Egg yolk material is now produced by one of the commercial companies, and if it turns out well there will be another convenient method of diagnosing lymphogranuloma.

In answer to Dr. Bernstein's question as to how early the reaction to a Frei test is positive, there are varying reports in the literature. Some observers state that the reaction becomes positive when the inguinal lymph nodes become attached to the skin. This is not true. On the other hand, the exact date is hard to estimate. I think any time within six weeks of infection is probably correct. In less than nine days one is apt to get some positive and some negative reactions. To be on the safe side, I should say more than nine days and probably within six weeks after infection has taken place.

Since September 1939 I have treated successfully 35 patients with this disease and with involved inguinal glands.

Syphilitic Glossitis; Smooth Atrophy; Leukoplakia with Early Malignant Changes. Presented by DR. GIRSCH D. ASTRACHAN.

D. L., a man aged 65, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 15, 1940. At that time he presented a partial smooth atrophy of the tongue, leukoplakia and a raised, partly ulcerated verrucous growth which involved the entire left half of the lower

lip. A biopsy specimen was taken from this lesion, and the diagnosis was prickle cell epithelioma. The patient was referred to the radiologic department, where radium therapy was administered. After the lesion on the lip healed, the patient was treated in the dermatologic clinic and received ten injections of a bismuth compound and potassium iodide by mouth.

On Jan. 7, 1941 he complained of a slight pain in the cheek. Examination revealed a dime-sized, raised, verrucous lesion on the inner surface of the right side of the cheek. Histologic examination revealed leukokeratosis with early malignant changes, and the lesion was destroyed by electrodesiccation.

At present the patient presents a nickel-sized, slightly ulcerated area on the right side of the cheek near the corner of the mouth. The surface of the tongue and the buccal mucosa, especially near the angles of the mouth, present a grayish blue discoloration. The leukoplakia is diffuse in some areas and has a bandlike configuration in others. The papillae are absent on a large area of the tongue; the surface is smooth and lobulated by fissuring. On the right side of the lower lip there is some scarring. The submaxillary glands are slightly enlarged.

The Wassermann reaction of the blood was positive on repeated examinations. The urine was normal except for giving a slight reaction for albumin. A complete blood count was normal. Examination of the heart revealed dilatation of the aorta and evidence of myocardial changes.

The microscopic diagnosis was leukokeratosis with early malignant changes in a person with syphilis. The epidermis was tremendously and irregularly acanthotic. The palisade layer was intact; the surface was verrucous, covered by a pronounced increased horny layer which was densely packed. In some areas the horny layer dipped deep into the epidermis. In the lower portion of the epidermis there was some anaplasia, a suggestion of whorl formation and some dyskeratosis. Throughout the upper part of the cutis and extending into the epidermis there was a tremendous cellular infiltration. Throughout this zone and throughout the midcutis were numerous small dilated blood vessels. The cellular infiltration was composed of small round and plasma cells. Some of the vessels in the intima were swollen, and in some areas the lumen was almost obliterated.

DISCUSSION

DR. GIRSCH D. ASTRACHAN: This case is presented in order to demonstrate various after-effects of untreated syphilis and the relation of syphilis to cancer. The question arises: What should be the next form of treatment in this case? Should further therapy be administered to the region where a beginning malignant condition was found? Should prophylactic roentgen ray therapy be given to the neck? What further antisyphilitic therapy is indicated?

DR. FRED WISE: It has been my experience that patients with a malignant condition of the tongue and of the buccal mucosae should not take arsenic. The tongue should be treated for cancer, and the syphilis should be left untreated, or if antisyphilitic treatment is given arsenic should be omitted.

DR. ISADORE ROSEN: I have seen several patients in whom epithelioma of the tongue or cheeks developed on a syphilitic base. After the epitheliomatous infiltration was thoroughly removed, I insisted on treating these patients with a bismuth compound only and with iodides during the rest periods, repeating this treatment in courses over a period of years. I have been able to follow these cases as long as eleven years without any evidence of recurrence or metastasis. It is my opinion that patients who have cancer on a syphilitic base and who are treated thoroughly with a heavy metal only, after removal of the lesion, have a better prognosis than nonsyphilitic patients. I agree with Dr. Wise that patients with syphilitic lesions of the tongue should not receive arsenicals of any kind. This advice is based on a long experience in the treatment of patients with neurosyphilis who had an associated glossitis or leukoplakia and who were treated intensively with the arsenicals to control the infection of the neuraxis. In some

of these patients rapidly evolving cancers of the oral cavity developed, and the patients succumbed not to the syphilitic infection but to the malignant growth.

DR. CHARLES WOLF: One of the desiderata of treatment of cancer of the oral cavity in syphilitic patients is local hygiene. I stress hygiene of the mouth, which, in the vast majority of patients will suffice until death occurs from other causes, viz., metastases, provided the local disease is properly treated. Smoking must be interdicted. The teeth and all existing infection must be taken care of. The question whether one may use arsenic or bismuth or potassium iodide must be individualized, provided the epithelioma is treated properly by physical agents.

DR. GEORGE C. ANDREWS: One other point in this type of case concerns the supplemental use of nicotinic acid and other vitamins. One ordinarily thinks of nicotinic acid and vitamin B as being useful in lesions of the tongue in avitaminoses but not in syphilitic leukoplakia. I have seen benefit from the internal use of nicotinic acid in patients with precancerous lesions of the tongue of late syphilis. It does not influence all patients favorably, but it does some. It is reasonable to suspect syphilitic patients of having hepatic damage; they are often alcoholic addicts and may have some vitamin deficiency along with their syphilitic disease.

DR. E. WILLIAM ABRAMOWITZ: Lane, of Boston, suggested the use of an estrogenic substance in leukoplakia, which is favorably influenced, whereas no effect is observed in lichen planus of the mouth.

DR. GIRSCH D. ASTRACHAN: In closing I should like to mention the fact that according to White (MacKee, G. M., and Cipollaro, A.: Cutaneous Cancer and Precancer, *Am. J. Cancer*, 1938, p. 44), 60 per cent of a series of patients with leukoplakia had syphilis and all used tobacco.

In answer to the question of the use of arsenicals in this case, I agree with Dr. Rosen and Dr. Wise. I believe little can be achieved even with an arsenical in a patient with established atrophy of the tongue, glossitis and a definite leukoplakia involving the greater part of the buccal mucosa. The possibility of activating buccal cancer has to be considered. This patient has been receiving bismuth injections and potassium iodide, and the same therapy will be continued. There was never any question of giving arsenic to this patient, because he is 64 years old and presents an aortitis and definite myocardial changes.

A Case for Diagnosis (Extracellular Cholesterosis?). Presented by DR. OSCAR L. LEVIN.

B. P., a woman aged 50, a Russian Jewess, stated that she first observed the eruption of the hands in June 1940. She appeared at the Mount Sinai Hospital dermatologic clinic on June 10, presenting firm red lesions, varying in size from that of a pinhead to that of a pea on the dorsa of the hands. The impression was that she might have had a form of erythema multiforme. She also presented dermatophytosis of the feet and dermatitis hemostatica of the legs. She visited the clinic on several occasions, and when observed on Jan. 31, 1941 she complained of the persistence and increase in the number of lesions of the hands and fingers.

Examination reveals a dozen or more grape-seed-sized to large pea-sized papules. These vary from dark red and purplish red to a slightly brownish red. They are most evident on the dorsa of the hands and there are a few on the proximal parts of the fingers. The smaller ones are dark red, rounded and irregular in shape. Some show flat tops with umbilication, and some present central translucent spots suggestive of vesicles. The larger lesions show central depressions, scaling and a tendency toward necrosis, and the largest ones show necrosis with crusts. The largest lesion is on the second metacarpophalangeal joint. This shows crusting and exaggeration of all the other signs. All the lesions feel firm. Some are present on the flexor aspects.

The past history indicates that the patient was treated for dermatitis venenata in May 1932. In 1935 she was treated for varicose veins and arthritis in the orthopedic department, and she was in the hospital in 1936 for pneumonia. On June 15, 1936, a roentgenogram of the chest revealed a few residual inflammatory areas of the lungs. In September 1937 she was treated for furuncles of the left leg, and in June 1939 she complained of a right femoral hernia.

DISCUSSION

DR. EUGENE TRAUGOTT BERNSTEIN: In my opinion the patient shows coincidentally two conditions, one a dermatophytosis with vesicular lesions on the hands and the other featuring pea-sized yellowish nodular lesions. I cannot be convinced that the case is one of the extracellular cholesterosis described by Urbach, Epstein and Lorenz (*Dermat. Ztschr.* **66**:371-386, 1933). The patient whose condition these authors investigated was first presented by Kerl (*Zentralbl. f. Haut- u. Geschlechtskr.* **36**:37, 1931) before the Vienna Dermatological Society in 1930 as exhibiting "multiple nodule formation containing much lipoid."

C. W. Laymon reported a case of extracellular cholesterosis (ARCH. DERMAT. & SYPH. **35**:269 [Feb.] 1937) in 1937. A girl aged 16 had an eruption which had appeared when she was 5 years old. It started with vesicles which coalesced and formed large nodules, especially on the backs of the hands, on the knees and around the ankles.

Of course, it is impossible to make a diagnosis here because this can be made only on the grounds of histologic evaluation. The difference between xanthoma and extracellular cholesterosis consists of the absence of large foamy cells and giant cells.

I propose two other diagnoses: (1) a coincidence of an "id" reaction from the dermatophytosis on the feet and (2) a condition described by Riehl and Arzt, xanthoma areolare multiplex. The latter condition is characterized, as in this case, by grouped, firm, brownish red or yellowish nodules which usually show central involution and atrophy and are surrounded by a pigmented halo. The lesions, also as in this case, often become pustular, but to differentiate between this type of xanthoma and extracellular cholesterosis on purely clinical grounds is impossible. However, the histologic picture of xanthoma areolare multiplex is characterized by the presence of the usual foam and giant cells which contain lipoid, a feature entirely absent in extracellular cholesterosis.

DR. FRED WISE: The eruption is suggestive of the condition mentioned by the presenter. I agree with Dr. Bernstein's statement that one cannot make a diagnosis in this case until the histologic report is submitted.

DR. OSCAR L. LEVIN: This case is unique. Of course, as suggested by a previous speaker, the patient has dermatophytids of the hands. The other lesions are hard—almost stony—and the central part of a few is translucent, suggesting the presence of fat in the tissue. Xanthoma tuberosum should be excluded. I believe that extracellular cholesterosis belongs in the group of xanthomas. In the case described by Urbach the point was made that foam cells are absent and the cholesterol is found outside of the cells. Hypocholesteremia rather than an increase in cholesterol occurs in the blood. In this case there is no evidence of diabetes; there was no sugar in the urine, and the blood sugar was normal. There may be evidence of hepatic disease, and in differentiating from xanthoma there may be a change in the ratio of the cholesterol to the cholesterol ester.

NOTE.—A subsequent histologic examination was made. The empty spaces in the cutis, their shape, and the presence of foreign body giant cells suggest extracellular cholesterosis. The pathologist also suggested that another biopsy specimen be sent to him for special staining. At this time also the urine was normal except for showing a few urate crystals and an occasional hyaline cast. The blood sugar amounted to 80 mg. per hundred cubic centimeters and the total cholesterol to 160 mg.

GEORGE C. ANDREWS, M.D., *Chairman*

HERMAN SHARLIT, M.D., *Secretary*

March 4, 1941

Primary Inoculation Tuberculosis of the Skin with Involvement of the Regional Lymph Nodes. Presented by DR. FRANK VERO.

B. L., a 28 year old physician, born in the United States, was first seen in the dermatologic clinic of Lincoln Hospital on Feb. 10, 1941. About twelve weeks previously he had noticed above the bend of the right elbow a pea-sized infected lesion (apparently contracted while performing an autopsy), which was soon followed by enlargement and tenderness of the axillary glands. The lesion on the arm was opened with a sterile needle, but only a minute quantity of pus was obtained. He received short wave diathermy treatment to the glands and then roentgen ray treatment (600 r), and finally the gland was incised and some thick yellow pus was obtained. The lesion on the arm failed to heal and grew gradually larger. The patient has been in good health. A tuberculin test last year gave negative results. A roentgenogram of the chest showed no evidence of tuberculosis or other abnormality.

The lesion on the arm is small, round, sharply defined, slightly raised, infiltrated, nodular and about 1.5 cm. in diameter. The color is a yellow-red-brown. In the center is a small depressed atrophic scar, and there is slight scaling and crusting in one area. On diascopic pressure there is no evidence of any apple jelly nodules. The surrounding skin appears normal. There is no evidence of acute lymphangitis except for a thin, cordlike band which can be seen and palpated on extension of the arm. The axillary glands are enlarged and infiltrated and appear to be packed together in one large mass without any inflammatory changes of the skin but with some tenderness on palpation. From a small opening (site of incision) a scanty thin yellowish pus can be expressed. There is no evidence of any other glandular involvement or of other cutaneous manifestations.

The dark field examination showed no Spirochaeta pallida, and the Wassermann reaction of the blood was negative. A tuberculin patch test elicited a positive reaction, and intradermal injection of tuberculin in a dilution of 1:100,000 elicited a positive reaction. Culture of material from the glands was negative for fungi.

The entire lesion was excised. Half of the specimen was used for animal inoculation, the result of which is not yet known. The other half was an excised fragment of epidermis, triangular and measuring, fixed, 1 by 0.7 by 0.4 cm. There appeared to be mild subcutaneous thickening. No gross pigmentation was evident.

Microscopic examination revealed a granulomatous process involving the entire thickness of the corium and at several points ulcerating through the epidermis. The lesion was fairly sharply circumscribed. It consisted of syncytial masses of poorly defined but elongated cells with semivesiculous nuclei—cells of the "epithelioid" type. In places a whorl-like arrangement of these cells suggested tubercle formation. These masses were ringed by rows of Langhans' giant cells. There was a moderately profuse lymphocytic infiltrate surrounding them. Several small foci of caseation necrosis were present. There was no fibrosis. Staining with hematoxylin and eosin showed no evidence of bacteria or of fungi. The epidermis over the lesion was thinned and in places eroded. Elsewhere it showed mild acanthosis. No doubly refractile material was made out. The provisional diagnosis was chronic granuloma of the cutis.

DISCUSSION

DR. A. BENSON CANNON: When I saw this patient with Dr. Vero a few weeks ago, I suggested the diagnosis of primary tuberculosis of the skin with a tuberculous abscess of the axillary gland. My reasons for suspecting tuberculosis were: first, the evident granulomatous character of the lesions; second, the fact that the

patient was a physician performing frequent necropsies; third, that the primary lesion appeared above the gloved hand, and, last, the walled-off abscessed glands. Furthermore, I had seen a similar condition in a medical student, whose primary lesion was an indolent ulcer on the tip of one finger with the same type of abscessed glands in his axilla. Agglutination tests for tularemia gave negative results. A specimen from the finger, as well as one from the axillary glands, showed the characteristic histologic structure of tuberculosis, and guinea pig inoculations for tuberculosis gave positive results. Surgical removal of the affected parts resulted in primary union and a cure of the infection, so far as I could determine. I suggested to Dr. Vero in this case that biopsy specimens be taken from the initial lesion and from the gland, that guinea pig inoculations be made with the tissue removed from both areas and that subsequent excision of the affected parts be performed. Dr. Vero's case impresses one with the necessity for differentiating between tuberculosis, primary initial lesion of syphilis and tularemia in all similar cases. I do not believe that tuberculosis of the skin and secondary abscesses of the adjacent glands are difficult to cure by surgical removal. So far as I know, there is seldom tuberculosis of vital tissues and organs when the primary and secondary foci have been removed as described.

Epithelioma of the Penis. Presented by Dr. Frank Vero.

P. H., a white man aged 69, was first seen in the dermatologic clinic of the New York Polyclinic Medical School and Hospital on Jan. 20, 1941 because of a penile ulcer. He stated that about four weeks previously he had noticed a small ulceration on the glans, which spread rapidly to the sulcus and prepuce. He gave no history of any venereal disease.

On the glans penis extending toward the frenulum, the sulcus and the inner surface of the prepuce there were extensive erosions and deep ulcerations, the borders of which were hard and rolled. The base of the ulcer was covered with a yellowish greenish purulent exudate. In some areas there were raised papillary projections with bleeding points. The entire prepuce was edematous and hard and could be retracted only with difficulty. The right inguinal glands were somewhat enlarged, hard and not tender. The Wassermann reaction of the blood has been negative on two occasions.

Microscopic examination of tissue from the prepuce showed a portion which presented an inflammatory reaction, ulceration and a profound degree of epithelial hyperplasia with epithelial downgrowths. The inflammatory reaction centered particularly around some of the smaller blood vessels, and the possibility of a syphilitic lesion had to be excluded. Many eosinophils were seen in some areas. In spite of the fact that syphilis may produce a decided degree of epithelial hyperplasia it seemed that a diagnosis of epithelioma was justified. The patient received five intramuscular injections of bismuth subsalicylate without any improvement. During the last ten days he was given roentgen ray therapy (500 r) to the penis and to the inguinal glands.

DISCUSSION

Dr. A. Benson Cannon: Dr. Vero is to be congratulated on making the diagnosis of epithelioma in this case. I should not have suspected such a condition from the clinical appearance and because of the short duration of the lesion. The sclerosis involves the entire circumference of the prepuce in a bandlike formation, much as does chancre. There is no ulceration, although inflammation is present and there is a little discharge, as though caused by irritation from medication. I have never seen an epithelioma of the prepuce without ulceration or leukoplakia or both.

Dr. Charles Wolf: From a superficial examination my impression is that this condition is not cancer. It is one of the varieties of venereal infection. This man may have syphilis, in spite of negative clinical findings. I suggest that the presenter study the case from the standpoint of venereal disease—if not syphilis,

perhaps chancroid or granuloma inguinale. Inconclusive examination of the tissue does not warrant the treatment as administered.

DR. MAX SCHEER: My clinical impression is that this patient has a gumma of the penis. The five injections of bismuth subsalicylate he has had may be insufficient to get rid of the lesion or even to reduce it. I suggest administering large doses of iodides for a few weeks to see what happens to the lesion.

DR. GEORGE C. ANDREWS: My own experience with epithelioma of the penis has shown that it is a serious disease and one that I should prefer to have treated by a genitourinary specialist rather than by a dermatologist.

DR. FRANK VERO: At the tumor clinic of the New York Polyclinic Medical School and Hospital a diagnosis of epithelioma was made. The lesion was hard at the beginning, but it has diminished since the institution of roentgen ray therapy. I thought of the possibility of a gumma, but the patient has no history of syphilis; he has six children, who are all healthy, and the Wassermann tests performed in the past all have given negative results, as have the two recent ones. He showed no improvement under antisyphilitic therapy; in fact, the lesion has spread during treatment. It is rather unusual for an epithelioma to spread so rapidly in two and a half months, but I do not know whether one can accept the accuracy of the patient's history.

NOTE.—The reaction to another Wassermann test has been reported as negative, and examination failed to show any evidence of secondary syphilis. The patient has received large amounts of potassium iodide and bismuth subsalicylate without any improvement. A surgical amputation was performed, and the diagnosis of epithelioma of the penis was verified by subsequent histologic examination.

Dermatitis Exfoliativa (Arsenical). Presented by DR. A. BENSON CANNON.

L. A., a white man aged 60, was admitted to New York City Hospital, Welfare Island, in October 1940 with a history of a generalized cutaneous eruption of four months' duration. He stated that scaly lesions appeared on the flexor surfaces of both forearms and ankles and spread so that now the entire body is covered. There has been much weeping and itching.

The patient is a presser, and he states that fumes from the cleaned clothes are all about the room in which he works. He did not work for five weeks before admission, but in spite of this the dermatitis became worse. There is no history of allergy. He has been using Coffelt hair tonic for ten years.

The entire body is covered with an erythematous hyperkeratotic rash with a leathery consistency. There is a moderate amount of scaling, with small bleeding points from the denuded areas. With the exception of edema of the ankles, the rest of the physical examination showed no abnormalities. The Wassermann reaction of the blood was negative, and examination of the urine for arsenic gave negative results. The arsenic content of the blood was 0.10 mg. per hundred grams of blood. Roentgen ray examination of the lungs and heart showed no abnormalities. It was reported that the histologic examination showed psoriasis.

The patient has received ammonium chloride, 20 grains (1.3 Gm.), for two months and sodium thiosulfate intravenously every other day. He has also been given various prescriptions containing solution of aluminum acetate N. F., menthol, camphor, solution of coal tar N. F., ichthammol, tragacanth, etc., without beneficial result. At present he is being treated with roentgen rays, ultraviolet irradiation and powder.

Dermatitis Exfoliativa. Mycosis Fungoides? Presented by DR. A. BENSON CANNON.

J. S., a white man aged 68, was admitted to New York City Hospital, Welfare Island, on May 13, 1940 because of swelling and ulcerations of both legs. The

patient had had a dry, scaly skin for eighteen years before admission. A biopsy performed at another hospital in 1937 was said to show mycosis fungoides. He was given numerous courses of roentgen ray therapy, and the lesions cleared up to a great extent.

Examination on admission revealed an extensive abscess of the left leg and pneumonia of the lower lobe of the left lung, in addition to the condition of the skin. There were separate and confluent patches of dry scaly reddish brown lesions with some infiltration, considerable lichenification and numerous excoriations.

The abscess of the leg was drained, and a hemolytic streptococcus was found to be the causative organism. The hemoglobin on admission was 45 per cent, and the patient was given a blood transfusion. After his recovery from pneumonia the condition of the skin improved somewhat.

The blood count and the urine were normal. The Wassermann and Kahn reactions of the blood were negative.

The itching has now returned, and the lesions have become more prominent.

DISCUSSION OF TWO CASES OF DERMATITIS EXFOLIATIVA

DR. EUGENE TRAUGOTT BERNSTEIN: I examined the first patient about three months ago. The question was raised then as to whether or not the dermatitis was due to an occupational exposure. He was sick when I first saw him but appears to be greatly improved now. He impressed me as having generalized dermatitis exfoliativa with a previous history of psoriasis. The histologic picture revealed the typical features of psoriasis. I reported to the insurance company a diagnosis of dermatitis exfoliativa with a microscopic picture of psoriasis. In my estimation there was no relation between the patient's condition and his occupation.

DR. HERMAN SHARLIT: The first patient consulted me about two and a half years ago for a lesion on the penis, which was typical psoriasis, and I treated him as I treat all patients with psoriasis of the penis: I told him to forget it. He was not given arsenic, and he accepted my advice. Later he came to me with nothing else but dermatitis venenata on the legs, and he was given a bland ointment; within two weeks exfoliation of the skin began which I could not control, and he had to be hospitalized. Although he was given no arsenic, he did use hair tonic. The arsenical value in the blood is not high; possibly this arsenic is the background for the dermatitis, but it is a fact that the patient is a psoriatic person. What the psoriasis has to do with the present condition I do not know, but I feel that persons with psoriasis are particularly prone to this type of eruption. It may be that in this case there is evidence that exfoliation in a person with psoriasis comes from arsenic.

DR. LOUIS TULIPAN: I encounter cases at Bellevue Hospital frequently in which exfoliative dermatitis has followed psoriasis, and usually it is due to some application. Applications of chrysarobin frequently start a dermatitis which may result in generalization and exfoliation. It is possible that this man may have used something else, in spite of the fact that Dr. Sharlit gave him only bland ointment. Dr. Sharlit has verified the fact that the patient has psoriasis, and I think the entire condition is a picture that is seen fairly often in the course of that disease.

DR. ADOLPH ROSTENBERG: I feel convinced that arsenic can cause exfoliative dermatitis in patients with psoriasis. I remember vividly the case of a patient who lived in Mexico, where he received injections of arsphenamine for psoriasis. He told me he was very sick afterward and described his condition as a severe exfoliative dermatitis. Later the psoriasis recurred, and I treated him cautiously with a few roentgen ray exposures and arsenic in the form of asiatic pills. Again a severe type of dermatitis exfoliativa developed with complete shedding of nails and hair. I gave him sodium thiosulfate, and he improved so much that it made me a strong advocate of that drug.

DR. DAVID BLOOM: It will be of interest to the presenter that I have recently had excellent results in the treatment of erythroderma psoriaticum with liver extract and a yeast concentrate.

DR. E. WILLIAM ABRAMOWITZ: I do not think the statement should be put on record that in every case of psoriasis in which a generalized exfoliative dermatitis develops the condition is due to the use of irritating local applications or to some internal medication. Psoriasis may become generalized, with profuse redness and scaling of the entire body—a so-called erythroderma psoriaticum. This happens frequently without any ascertainable cause. I had a patient who gave a history of six such outbreaks during thirty years. I observed him in the last outbreak, and I know that there was nothing that he used which could be blamed for this development. There are, of course, cases in which a generalized dermatitis develops from local treatment.

The amount of arsenic reported found in the blood of this patient, 0.1 mg. per hundred cubic centimeters, may be within the upper limits of the normal range, depending on his diet and other factors, especially the hair tonic that he was using.

Regarding the effects of sodium thiosulfate: the recent literature (Mattice, M. R.; Baxt, H., and Byrne, J. M.: ARCH. DERMAT. & SYPH. **42**:399 [Sept.] 1940) indicates that the amount of arsenic excreted may be suppressed by the use of this drug. Work is being done by Mattice, Botwinnick and myself which shows that this may also apply to other heavy metals, like bismuth and gold. I therefore recommend that this patient be given a high carbohydrate diet with injections of liver extract instead of sodium thiosulfate.

DR. LEWIS B. ROBINSON: I understand that the patient was using hair dye, not hair tonic, in which case he could well have hair dye dermatitis on a psoriatic skin.

DR. A. BENSON CANNON: I doubt whether one is able to make a diagnosis of psoriasis on a penile lesion alone, as Dr. Sharlit has done in this case. I have seen a number of patients with scaly plaques limited to the glans penis, conditions which had been diagnosed as psoriasis, but I have never known any of these patients to have lesions of psoriasis elsewhere. In a number of cases of this kind I have been able to prove the lesion on the penis due to a contact dermatitis. I think it is sometimes difficult to say whether an eruption is due to arsenic, even though one finds an abnormal amount in the blood. I consider the normal value for blood arsenic to be from 0 to 0.05 mg. per hundred cubic centimeters when there has been no history of intake of the drug, and this determination has been confirmed by numerous tests. I believe that sodium thiosulfate and calcium thiosulfate increase the elimination of arsenic, as was shown first by Drs. Fordyce, Rosen and Myers many years ago and by numerous tests my associates and I have done in the last fifteen or twenty years. In cases of jaundice due to arsenic one often notes that the administration of sodium or calcium thiosulfate causes a gradual decrease in the intensity of the jaundice, a decrease in the bile index and an increase in the arsenic content of the urine.

DR. OSCAR L. LEVIN: The patient shows a generalized erythroderma. The history and the histologic report from the New York Post-Graduate Medical School and Hospital indicate that the patient had mycosis fungoides, and the diagnosis should be accepted as presented. An important clinical point is the presence of generalized erythroderma enclosing spots of apparently normal skin. I have always felt that the presence of such spots tends to confirm a diagnosis of mycosis fungoides.

DR. A. BENSON CANNON: So far I have observed no lesion that could be ascribed to mycosis fungoides.

Purpura Annularis Telangiectodes. Presented by DR. JAMES L. MILLER.

C. S., a man aged 65, is presented from the dispensary of New York City Hospital, Welfare Island, complaining of an eruption on the legs which has been

present for seven months. The patient first noticed an itchy red spot about the size of a quarter on the left shin. This gradually cleared, leaving a brownish pigmented area. In the meantime new pea-sized lesions appeared on the same leg and later on the opposite one. The only treatment used was a salve.

Examination shows pea-sized to dime-sized, red to violaceous, macular areas scattered over the left leg from the knee to the ankle. These areas are made up of telangiectases and do not fade on pressure. No atrophy is noted in areas where several lesions have cleared, leaving only brownish pigmentation.

The past history is irrelevant except that there was an attack of pleurisy with effusion in 1907, followed by frank tuberculosis in 1916, which required hospitalization for ten months. The patient suffered a relapse in 1921 but has remained well since. In 1934 he broke his left leg. This was treated with reduction maintained by steel pins in the left knee, and motion is still limited in this knee.

The patient states that he has had no medication except liquid petrolatum and a liver and stomach extract with iron (lextron).

DISCUSSION

DR. OSCAR L. LEVIN: I do not believe the patient has purpura annularis telangiectodes (Majocchi's disease). He shows widespread telangiectases, petechiae, slightly elevated hemorrhagic papules and small angiomas, as well as pigmented spots. I believe the condition is angioma serpiginosum. There are no annular lesions and no atrophy, which should be present in purpura annularis telangiectodes.

DR. GEORGE C. ANDREWS: I do not agree with either of the diagnoses. I think the condition is purpura simplex. I recommend that a platelet count be made.

DR. MAX SCHEER: I am one of those who cannot agree with the diagnosis of purpura annularis telangiectodes. A number of patients have been presented with that diagnosis, and none of them has shown sharp, distinct annular lesions with central atrophy. The disease with which I would classify the condition in this case is that described several decades ago by Klotz as dermatitis hemostatica.

DR. EUGENE TRAUGOTT BERNSTEIN: I think the condition is Osler's disease, with angiomas and purpura of the symptomatic type.

DR. HENRY D. NILES: The lesions are too elevated to be simple purpura or dermatitis hemostatica. As far as angioma serpiginosum is concerned, the lesions are not serpiginous any more than they are annular.

DR. OSCAR L. LEVIN: The patient shows no evidence of dermatitis hemostatica. Dermatitis is not present. The condition is due to changes in the smaller vessels of the skin. The term angioma serpiginosum is a poor one; the condition does not necessarily have to be serpiginous in outline, and satellite lesions may be present.

Lichen Sclerosus et Atrophicus (Hallopeau). Presented by DR. DAVID BLOOM.

E. B., a woman aged 43, was previously presented before the Bronx Dermatological Society in February 1941 (ARCH. DERMAT. & SYPH.).

Lichen Sclerosus et Atrophicus (Hallopeau). Presented by DR. BENSON CANNON.

S. V., a white woman aged 57, is presented from Vanderbilt Clinic with an eruption which has been present for a year and a half. She was seen today for the first time.

The condition began over both clavicles. The patient did not know of the lesions on the back of the neck, but for the last week she has noticed that the eruption was appearing in the cubital fossae. The only symptom noted by the patient has been dryness. There has been no itching, pain or paresthesia.

The patient has chronic bronchiectasis.

Examination reveals pinhead-sized to split pea–sized lichenified papules, definitely atrophic, on the back of the neck. The lesions in the clavicular areas are atrophic, dry and scaly, with some irregular increase in pigmentation. There are a few follicular plugs and some telangiectasia. Small, discrete and grouped atrophic lesions are present in both cubital fossae.

Lichen Atrophicus. Presented by DR. E. N. BOCCANEGRA LOPEZ.

H. M., an American-born white woman aged 46, is presented from the department of dermatology and syphilology of the New York Polyclinic Medical School and Hospital with a rash involving the right supraclavicular region, lower part of the neck and upper part of the back of two years' duration. The patient states that the lesions appeared first in the right supraclavicular region and soon after on the upper aspect of the back and neck as scattered papules which extended peripherally and atrophied in the center. There was not much itching, pain or discomfort.

Examination of the back of the neck reveals a large patch of livid atrophic dermatitis, which appears to be formed by a fusion of individual angular papules. This patch has an irregular border and is surrounded by a pinkish halo up to about 1 cm. in width. At the periphery minute keratotic plugs can be detected in the follicles. On the right and left sides of the neck there are also atrophic lesions of the same character, but these are surrounded by numerous satellites of atrophic papules. A few whitish patches are observed on the oral mucous membrane, particularly on the right side.

Histologic examination of tissue from the lesion on the right side of the neck confirmed the diagnosis of lichen atrophicus.

Treatment has consisted of local application of boric acid ointment, and a small patch on the right side of the neck was selected for the intraepidermal injection of procaine hydrochloride and epinephrine, as suggested by Morgan and Dennie (ARCH. DERMAT. & SYPH. **43**:157 [Jan.] 1941), with promising results.

DISCUSSION OF THREE CASES OF LICHEN

DR. EUGENE TRAUGOTT BERNSTEIN: The last patient presented had lesions of lichen planus in the mouth, and the question arises whether there is a connection between lichen planus and lichen atrophicus. Montgomery and Hill (ARCH. DERMAT. & SYPH. **42**:755 [Nov.] 1940) stated the belief that there is no connection, but I think lichen atrophicus or lichen sclerosus is lichen planus which occurs in a patient who is apt to react with atrophy.

DR. DAVID BLOOM: In some of the cases I have observed which were definitely instances of lichen sclerosus et atrophicus there were violaceous papules. In other cases, as, for instance, the one presented by me, these papules are not present. I believe that the condition in the third case (presented as one of lichen atrophicus) belongs to the same group as that in the other 2. The presence of linear whitish lesions on the buccal mucosa does not prove that the condition is lichen planus. The oral lesions may be of the same nature as the cutaneous lesions. Histologic examination of the oral lesions and of those on the skin would be of value.

DR. HENRY D. NILES: I agree with Dr. Bloom that in Dr. Lopez' case the lesions in the mouth might be part of the process. Montgomery and Hill described lesions of the vulva and of the penis. In fact, lesions occur rather frequently on the vulva. I cannot agree at all with the concept of Dr. Bernstein that lichen atrophicus may follow lichen planus. In the former condition the lesions are white and atrophic from the beginning, and one never sees typical lichen planus lesions first. If one follows the case for several weeks or months new lesions can be seen appearing, but they are white from the beginning and gradually enlarge. Another interesting feature is that in these 3 cases the patients are all women, about middle age, with lesions chiefly on the upper part of the chest and on the back. This is usual, although one may see the condition in males and on other parts

of the body. The predilection is for the upper part of the trunk in middle-aged women, which leads to the assumption that there may be some underlying endocrine deficiency. It would be interesting to attempt therapy on this basis, treating these patients with estrogenic ointment. In view of the fact that there is no specific therapy, this treatment would be justified.

DR. DAVID BLOOM: In answer to Dr. Niles, my patient has been receiving estrogenic preparations for menopausal symptoms resulting from the removal of her ovaries one and a half years ago. In spite of this treatment new cutaneous lesions have appeared until recently.

DR. E. N. BOCCANEGRA LOPEZ: The diagnosis in my case was based on the clinical appearance of sclerotic degeneration of the skin which fused together and formed a large patch, and it was confirmed by histologic examination. I want to emphasize the disappearance of the lesion above the clavicle following the injection of procaine hydrochloride and epinephrine. I think it would be worth while to inject these substances around the edge of the present lesion to see if it will disappear.

Epidermolysis Bullosa Hereditaria. Presented by DR. HENRY D. NILES.

W. S., a boy aged 12 years, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 16, 1941.

The present illness started at birth with bullae at the site of even the slightest trauma. These were followed by scarring and gradual deformity of the hands and feet.

A maternal uncle has similar lesions. There have been four siblings, and two of these had similar lesions (one died at 2 weeks of age and one at 5 months).

Examination shows deformity of all the toes of the right foot and the fingers of both hands, although not to the same extent. There is partial deformity of the toes of the left foot. The skin of the hands and feet is atrophic and covered with crusts and scales at the sites of former bullae. There are similar lesions on the shins and the sides of the neck and similar, less severe changes scattered over the rest of the body. The fingers and toes are fused into clawlike deformities. There are many small milium-like cysts on the rim of each ear. There are also indentation of the tongue, a suggestion of saddle nose and disturbances in dentition.

Histologic examination of a specimen taken from the right elbow confirmed the clinical diagnosis. Roentgenologic examination of the hands and feet showed pronounced flexural deformities of both hands, webbing of the fingers and of the soft tissue over the toes of the right foot and underdevelopment of the osseous structures of the hands and feet.

DISCUSSION

DR. A. BENSON CANNON: I suggest treating the patient with autogenous vaccine and sulfanilamide. I have a patient at the Vanderbilt Clinic similar to this one who has virtually been cured with injections of streptococcus vaccine and administration of sulfanilamide.

DR. DAVID BLOOM: In spite of this disease being hereditary in nature, the treatment which has been suggested may in some unexplained way benefit the child.

DR. CHARLES WOLF: The child has mutilated membranes of the body. How can they be replaced? Epidermolysis bullosa hereditaria goes on to a terminal destructive effect. I see no indication for the administration of sulfanilamide.

DR. GEORGE C. ANDREWS: I do not think Dr. Wolf could have understood the remarks that were made. There is no question of replacing lost members. Dr. Cannon's contribution to this subject is, to the contrary, interesting and valuable.

DR. HENRY D. NILES: The suggestions for treatment are welcome and necessary. I do not expect to correct the deformities completely, but the orthopedic surgeons feel that they can accomplish something along that line, and they will not even attempt it until the overlying skin is in better condition. So, if that can be improved by using a vaccine or sulfanilamide or, as Ludy, De Valin and Hart-Drant (*M. Clin. North America* **16**:169, 1932) have done, by giving high doses of viosterol, I believe that I am certainly justified in trying all of those methods.

Lymphogranuloma Venereum. Presented by DR. GERALD F. MACHACEK.

L. F., a Negro aged 31, is presented from New York City Hospital, Welfare Island, with lesions of the penis, scrotum and pubic region of ten years' duration. He was first admitted on June 20, 1939 because of multiple ulcerative and suppurative lesions of these regions. The patient claims that the onset occurred ten years ago following trauma, incurred in a baseball game, which caused the scrotum to become swollen. Several weeks after the accident pustular and ulcerative lesions developed in the groins and on the upper part of the thighs.

For ten years the lesions have progressed, resulting in multiple sinuses and fissures in the pubic area and on the penis and scrotum, with a purulent discharge. There are tremendous enlargement and distortion of the penis, with beefy granulations, and circinate scarring of the inguinal region and of the thighs.

The Wassermann reaction of the blood was 4 plus; the Wassermann reaction of the spinal fluid was negative. The colloidal gold curve was 0011110000. The reaction to Frei and Ducrey tests have been repeatedly positive. A culture of material from the lesions showed staphylococci, streptococci and diphtheroid bacilli. The blood and the urine are normal.

The patient has had repeated courses of sulfanilamide, antimony and potassium tartrate, fuadin, fever therapy with malaria and typhoid vaccine and active antisyphilitic therapy. Local treatment has consisted of irrigations with N. F. antiseptic solution and phenol and application of the soothing ointments and sulfanilamide.

DISCUSSION

DR. DAVID BLOOM: Elephantiasis and fibrosis involving the penis and scrotum, as seen in this patient, are typical of granuloma inguinale. The presence of a positive Frei reaction does not prove that the lesions are those of lymphogranuloma venerum, for not infrequently in Negroes a positive Frei reaction is obtained without any apparent clinical manifestations.

DR. LOUIS TULIPAN: I think the only thing that can be done for this condition is either surgical excision or destruction of the entire mass with surgical diathermy.

DR. A. BENSON CANNON: Granuloma inguinale is regarded as a cutaneous disease and lymphogranuloma venereum as a lymphatic disease. I believe that one rarely, if ever, sees granuloma inguinale involving the glans penis, although the skin of the shaft of the penis, in the crotch and around the anus is frequently affected. This patient has an undermining of the soft parts of the suprapubic areas over the abdominal wall, with multiple sinuses, so that when one presses on the wall of the abdomen a thin, blood-tinged pus exudes from the sinuses. Furthermore, the patient has a positive Frei reaction, and Donovan bodies have not been observed in repeated examinations of material from the lesions. It is possible that the man may have granuloma inguinale in addition to the lymphogranuloma venereum.

DR. MAURICE J. COSTELLO: I presented a patient before the Metropolitan Dermatological Society last month (ARCH. DERMAT. & SYPH., this issue, p. 757) with complete destruction of the penis from granuloma inguinale. It would not surprise me if Dr. Machacek's patient were suffering from both granuloma inguinale and lymphogranuloma venereum.

MANHATTAN DERMATOLOGIC SOCIETY

J. FRANK FRASER, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Feb. 11, 1941

Psoriasis in a Syphilitic Person. Presented by DR. GEORGE M. LEWIS.

J. B., a man aged 43, first had an eruption on the left palm five years ago. The left sole became affected soon afterward, and the condition has not improved since then. For two years the right palm was also involved. There was no troublesome pruritus; some tenderness of the affected skin was present. Therapy from four physicians included various local medications, ultraviolet radiation and three hundred and sixty injections (presumably of trichophytin). The patient had continuous treatment for one and a half years for syphilis about ten years ago; three years ago a short series of injections of arsphenamine was administered.

No nails are involved. The interdigital tissues are unaffected. The left sole and to a lesser degree the right palm show a subacute erythematous keratotic and scaly eruption. There are no vesicles.

There was no obvious focus of infection in the throat. A carious tooth had just been extracted. The Wassermann reaction was 4 plus. Scrapings gave negative results for fungi both microscopically and culturally. Histologic examination of a specimen from the edge of the eruption on the side of the left foot showed the epidermis to be acanthotic, especially the rete pegs. In many places the suprapapillary plates were thin. There was a pronounced, densely laminated horny layer, and in several areas there was considerable parakeratosis. Several Monro abscesses were noted. In the papillary bodies and in the upper part of the cutis an extensive cellular infiltration was to be seen; this consisted of small round cells, wandering connective tissue cells and numerous plasma cells.

DISCUSSION

DR. ISADORE ROSEN: I agree with the diagnosis. While arsenic is often used in the treatment of psoriasis, it has no effect on the eruption in syphilitic patients. I have seen several patients with both diseases who were treated intensively for their syphilitic infection, with no effect on the psoriatic lesions.

DR. M. PAROUNAGIAN: As the histologic picture is that of psoriasis, the diagnosis of psoriasis in a syphilitic person must be accepted.

DR. GEORGE C. ANDREWS: I should not be willing to accept the diagnosis of psoriasis until the patient has had more thorough antisyphilitic treatment.

DR. HERMAN SHARLIT: After looking at the slide, this condition to me is psoriasis.

DR. MAURICE J. COSTELLO: I agree with the diagnosis as presented.

DR. WILBERT SACHS: The histologic picture under low power magnification is fairly typical of psoriasis. The only difficulty is the presence of plasma cells, and with plasma cells it is difficult to establish a diagnosis of psoriasis. The problem is to find out whether the patient has a psoriasiform syphiloderm or whether the condition is psoriasis in a person with syphilis. Because the deeper vessels showed no particular changes and no perivascular plasma cell infiltrate, I thought the diagnosis was psoriasis in a patient with syphilis.

DR. DAVID BLOOM: Besides the clinical appearance, the bilateral location and the long duration speak for psoriasis and against syphilis. Such a case of psoriasis is of interest to me because of the fact that the lesions are limited to the palms and soles for such a long time without affecting other areas of the skin. The lesions are usually resistant to antipsoriatic treatment.

DR. FRED WISE: I agree with the diagnosis as presented.

DR. SAMUEL PECK: I think that this patient has psoriasis. In this particular instance, in which the influence of the syphilis on the psoriatic picture is being considered, it probably would be of interest for me to report the effect that a blood dyscrasia would have on the histologic picture of a person with an eruption. In leukemia, especially of the acute type, the leukemic blood picture can be seen to play a definite part in the histologic changes of psoriasis or of any other eruption having an inflammatory component. In the case presented by Dr. Lewis the histologic picture of psoriasis has been changed by the syphilis.

DR. GEORGE M. LEWIS: It is of interest that the treatment which this patient received from four different sources for a supposed fungous infection consisted of injections repeated for many months. While I could not be sure of the material given by injection, I believe that it was trichophytin. The patient had adequate therapy for syphilis as judged by present standards.

Erythema Induratum with Involvement of the Forearm. Presented by DR. MAURICE J. COSTELLO.

A. L., a woman aged 18, was first seen by me in November 1937, at which time she showed two healed circular, depressed, smooth scars on the posterior lower third of the right leg and a silver dollar–sized, irregular ulcer with surrounding induration on the anterior surface of the leg. A dime-sized similar painful ulcer was located on the anterior surface of the right leg. The patient stated that she had had these lesions one year and eight months prior to her first visit to my office. A week later a dime-sized nodule developed on the left knee joint. It was indurated, painless and devoid of visible inflammatory signs. During the next few weeks, a similar lesion developed on the lower part of the right leg, and a dome-shaped bluish red nodule appeared on the dorsal surface of the left wrist. An intradermal test with old tuberculin in a 1:100,000 dilution elicited a 3 plus reaction after forty-eight hours.

The patient had three sisters; one died of pulmonary tuberculosis at Sea View Hospital. The patient's father and mother are living and well. A roentgenogram taken of the chest was normal. Intravenous injections of 50 mg. of gold sodium thiosulfate were given at weekly intervals, in addition to generalized ultraviolet radiation. Treatment consisted of the administration of filtered roentgen rays and rest in bed.

DISCUSSION

DR. DAVID BLOOM: Referring to the association of pulmonary tuberculosis with cutaneous tuberculosis, dermatologists are fortunate to be able to recognize tuberculosis of the skin and thus to suspect pulmonary involvement. I know a young woman with lupus vulgaris whose condition was recognized by a dermatologist who induced her to have her lungs examined. A moderately advanced pulmonary tuberculosis was thus detected and was arrested after she was hospitalized for one and a half years. This case shows the importance of a thorough examination of every patient with cutaneous tuberculosis.

DR. MAURICE J. COSTELLO: The unusual features were that the lesions were mostly confined to the anterior rather than to the posterior surface of the legs and there was a lesion on the left wrist. When a diagnosis of pulmonary tuberculosis is made, all the members of the patient's family and intimate contacts are examined routinely, roentgenograms of the lungs being taken. I think that it is just as important to do this when a patient has cutaneous tuberculosis.

Erythroderma Psoriaticum. Presented by DR. DAVID BLOOM.

R. S., a man aged 21, had had recurrent lesions of the skin since the age of 2 years. Between the ages of 13 and 17 the eruption was located on the flexures of the extremities. In 1938 his eruption was diagnosed for the first time as psoriasis,

and it responded well a year later to thirteen roentgen ray treatments. In March 1940 the patient had a generalized exfoliative erythroderma, for which he was hospitalized for several months.

He now presents a universal, erythematous, exfoliating, lichenified eruption from which only the backs of his fingers and toes and the palms and soles are free. The patient complains of severe pruritus which occurs in frequent paroxysms and is relieved by scratching.

Examination reveals besides the eruption only enlarged lymph glands, which are particularly increased in size in the inguinal region.

The blood count and the differential count were normal. The Wassermann reaction of the blood was negative. The microscopic examination of the skin showed the structure of psoriasis.

For the past six weeks the patient has received biweekly 3 cc. of liver extract (2 U.S.P. units per cubic centimeter) by parenteral injection and brewers' yeast orally, with definite improvement in objective and subjective symptoms. In addition he was treated with ultraviolet radiation.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I feel that for the treatment of this type of condition a 30 per cent sulfur ointment should be tried. I used it for arthropathic psoriasis that became exfoliative after injections of a gold compound. Thirty per cent sulfur in petrolatum stopped the itching and cleared up the eruption which had been resistant to other treatment. Another patient at the New York Post-Graduate Medical School and Hospital had received tar, boric acid ointment, chrysarobin and other local remedies before coming to the hospital, and he showed 75 per cent improvement from 30 per cent sulfur.

I presented a patient here on May 9, 1939 (ARCH. DERMAT. & SYPH. **41**:136 [Jan.] 1940) who had exfoliative dermatitis and psoriasis. The patient had had six outbreaks of exfoliative dermatitis during thirty years. I never saw him in the previous attacks. When he came to see me, I made a diagnosis of exfoliative dermatitis with psoriasis, which was later proved by histologic examination. Unfortunately, leukemia developed but even then the cutaneous lesions showed psoriasis histologically. This condition cleared up after the use of 30 per cent sulfur. The patient died later from leukemia.

DR. SAMUEL M. PECK: In spite of the fact that my experience covers only fifteen years, I have observed such cases. It has been my distinct impression that both local and general therapy have not been successful in these cases. I have seen improvement in some, but it could not have been attributed to therapy. Also I have seen dermatitis caused by 30 per cent sulfur ointment in a few patients. I find this therapy extremely difficult to carry out in ambulatory patients.

DR. FRED WISE: For eruptions of this kind I have had good results with the Goeckermann-O'Leary treatment, consisting of the application of mild tar or solution of coal tar ointments and ultraviolet radiation.

DR. SAMUEL PECK: One should be very careful in the use of terms. Exfoliative dermatitis and erythroderma psoriaticum are certainly not the same condition. The former might be a complication from the use of a heavy metal, or even arsenic, while the latter is a special type of extensive psoriasis and is not the result of therapy.

DR. HERMAN SHARLIT: It seems to me that if a disease has only cutaneous manifestations and no other organic manifestation, it must be called a cutaneous disease. Irrespective of what type of background it might have, the symptoms of this disease are only in the skin or its appendages.

Three years ago I saw a patient who had a few scaly lesions on the penis. I told him he had psoriasis and to forget about it. He came back two years later with a dermatitis venenata of his legs. I do not remember what I gave him, but

it could not be anything more than a bland dressing. Within two weeks he had a generalized exfoliating dermatitis. Persons with psoriasis have apparently a weakness that can demonstrate itself in a generalized eruption of the exfoliative type. This man had no psoriasis on the trunk at the time of the dermatitis, but I knew from the history that he had had psoriasis before.

DR. PAUL E. BECHET: I have frequently observed an extensive psoriasis change into a universal scaly erythroderma because of a severe dermatitis following the application of an irritant such as chrysarobin or strong ammoniated mercury ointment or from excessive actinotherapy. I have not seen this change occur without such a preexisting dermatitis. I am aware that it can occur independently, but I do not think that it does so often enough to warrant the name erythroderma psoriaticum, which in my opinion is confusing, as a scaly erythroderma from any other dermatosis cannot be differentiated from one following psoriasis.

DR. DAVID BLOOM: I was impressed with the result of the treatment, for not only has the severe pruritus diminished but also the erythema and exfoliation have decreased definitely. This improvement has resulted also in an improved mental attitude. As to the exciting cause of the erythroderma, I learned that the patient had applied resinol ointment to the skin for several weeks previous to the development of the present condition. Now he uses plain petrolatum and needs about a pound (450 Gm.) a day in order to feel comfortable. Should this method of treatment not lead to a perfectly satisfactory result I shall follow the suggestion of Dr. Wise and use the Goeckermann-O'Leary treatment.

A Case For Diagnosis (Maculopapular Eruption on the Face). Presented by DR. FRED WISE.

W. J. G., a man aged 47, was referred by Dr. S. Sprague in consultation. He presents an eruption of brownish red macules and faintly elevated, noninfiltrated papules, approximately 0.5 cm. in diameter, on both cheeks and on the nose. Most of them show a discoid outline, and a few are polygonal. They have been present for five years. On the left cheek are approximately twenty lesions, on the right cheek eight and on the nose three. There are no subjective symptoms. The buccal mucosae are unaffected. The patient's general health was good, and physical examination showed no abnormalities. The patient said that the lesions on the cheeks appeared five years ago and those on the nose two years ago. No new spots have appeared since then. The history with respect to drugs or medicines is normal.

The histologic section (examined by Drs. D. Satenstein and W. Sachs) showed necrosis with granulation tissue. Extending throughout the upper and middle parts of the cutis there was an abundant cellular infiltrate, composed chiefly of plasma cells and polymorphonuclear leukocytes. The center of the mass was necrotic and contained many small dilated vessels. Between these vessels there were a considerable increase of connective tissue and a diffuse fibroblastic infiltrate.

DISCUSSION

DR. ISADORE ROSEN: I suggest the possibility of either Boeck's sarcoid or lichen planus. The color and the features strongly suggest the latter. While lichen planus is not often seen on the face, it does occasionally occur in that location.

DR. GEORGE C. ANDREWS: I believe that clinically the eruption looks more like sarcoid than anything else. I recommend that a specimen for biopsy be taken from another lesion.

DR. GEORGE M. LEWIS: Several of the lesions were angular, giving the appearance of lesions following the embedding of a foreign body.

DR. WILBERT SACHS: I cannot offer either a clinical or a microscopic diagnosis, but I do know that if the histologic picture I saw was representative

of all the lesions, a diagnosis of lichen planus and of sarcoid would be ruled out. There were numerous plasma cells. In addition, there was nothing to suggest a tubercle. There was definite necrosis, which would not be found in the presence of the two diseases.

DR. SAMUEL PECK: I agree with Dr. Sachs that lichen planus and sarcoid can be ruled out by the histologic picture, which showed foreign body giant cells. The clinical picture does not suggest powder burns or the type of scarring due to falling on gravel. However, from the history and histologic observations I should be willing to make a diagnosis of a foreign body reaction.

DR. E. WILLIAM ABRAMOWITZ: I suggest a diagnosis of factitious eruption. The condition does not conform to anything else. The patient probably produced the eruption by picking.

DR. DAVID BLOOM: Clinically the eruption impresses me as sarcoid or tuberculid. Investigation in regard to sensitivity to tuberculin is necessary. As to the absence of corneal and pharyngeal reflexes, I believe that the value of this test has been exaggerated. Recently there was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital a man with ulcers on the heels which, because of the unusual appearance, were diagnosed as self inflicted. This man showed considerably diminished corneal and pharyngeal reflexes. Further investigation revealed a tumor of the lower part of the spinal canal to be the cause of the ulcerations. Lessening or absence of corneal and pharyngeal reflexes is probably found in many normal persons.

DR. PAUL E. BECHET: The lesions are apparently smooth, and there are no changes on the surface; so it is extremely hard to reconcile these findings with a diagnosis of a factitious eruption.

Ainhum. Presented by DR. WILBERT SACHS.

L. A., a Negress aged 31, was referred to me by Dr. Henry Friedland. About three years ago a fissure developed on the plantar surface of the left small toe and was accompanied with pain and swelling. The process subsided, but in the past year there has been soreness on walking. The patient was confined to bed for a few days when another fissure developed. This healed with boric acid wet dressings. At various intervals there has been a burning sensation of the feet. During this time only bland therapy has been employed.

The patient was born in Georgia but has spent most of her life in Jacksonville, Fla. She has been living in Newark, N. J., since 1934. She is married and has one child, and there is no history of miscarriages. No one in the family has a similar eruption. During childhood a fissure was present at the same site, but this readily responded to mild therapy. A tonsillectomy was performed in 1935. One year ago the Wassermann reaction was negative.

Examination shows a deep constriction on the plantar surface of the left small toe. The tissue is sclerotic on the lateral aspect above the fissure. Otherwise there is no visible change in the toe. The right small toe shows similar changes. The fingers are not involved.

The following roentgenographic findings were reported by Dr. Porais: "There is a diminution in size of the second phalanx of the small toe, but the bone does not show the usual manifestations of osseous atrophy. There is an early similar change in the second phalanx of the adjacent toe."

DISCUSSION

DR. DAVID BLOOM: Eight years ago Dr. Newman and I reported a case (ARCH. DERMAT. & SYPH. **27**:783 [May] 1933) of ainhum. We studied roentgenograms of the lesions. There were fragmentation, absorption and atrophy of the distal portion of the second phalanx of the fifth toe, the area which corresponded to the location of the fissure. Several cases have been described in which two or more toes were affected. Although in most of the cases reported the patients

were African Negroes and Hindus, the disease has also been described as occurring in Arabs, Mussulmen, Chinese and white persons. I suggest that Dr. Sachs advise the patient to have this toe removed. It will be in the interest of the patient, and it will be possible to study the tissues thoroughly.

DR. HERMAN SHARLIT: During the last war when there were many peripheral nerve injuries to observe, in many cases atrophy of the small bones of the fingers developed. Apparently the cause of the atrophy here is destruction or irritation of nerve fibers.

DR. MAURICE J. COSTELLO: I think that a parallel of this trophic disturbance is found in the atrophy of the fingers associated with pressure from a cervical rib.

DR. WILBERT SACHS: The report of the roentgenologist that this condition is not the type of atrophy usually found in bone, I believe, favors the diagnosis of ainhum. Nothing is definitely known about the cause of this disease. It occurs most frequently in the Negro race, although it may be found in the white race. It is also seen on the fingers. The interesting features about this case are that three toes are involved and there is no complete fibrous ring.

Dermatitis Venenata Due to Underwear (Shorts). Presented by DR. ISADORE ROSEN.

L. O., a boy aged 15, came to the New York Post-Graduate Medical School and Hospital Skin and Cancer Unit on Feb. 7, 1941 with an eruption on the neck, abdomen, thighs, genitals, buttocks, arms and face of seven days' duration.

The eruption is mostly on the genitals, abdomen and buttocks and to a less degree in the other locations. The penis is edematous, being three times the normal size. It is also erythematous and vesicular. The eruption in the other locations consists of erythematous papules which are partly discrete and partly confluent, forming large plaques.

The patient felt weak and complained of severe burning and pruritus. He gave a history of having worn new shorts starting Feb. 1, 1941 and another new pair since February 3. Twelve hours later an eruption started on the genitals. The patient for the past few days has felt sick and has been confined to bed.

Patch tests with the following materials on the right forearm elicited positive reactions: white and black cotton shorts and brown and white cotton shorts.

DISCUSSION

DR. MAURICE J. COSTELLO: I have an opportunity to see a number of patients suffering from this eruption at Bellevue Hospital, because they can afford only inexpensive shorts, usually purchased at the Army and Navy stores. The eruption usually appears on the areas of contact within forty-eight hours but may not appear for a week. Many patients, in addition to presenting an eruption limited to the area covered by the shorts, have lesions in other areas as a result of absorption. All of the patients I observed gave positive reactions to patch tests. The diagnosis in the beginning is confused with dermatitis venenata due to poison ivy because of the intense pruritus and swelling of the genitals.

DR. E. WILLIAM ABRAMOWITZ: Not every condition that assumes this bathing trunk distribution is due to shorts. I had an experience recently with a baker who became sensitized to flour because he used a flour sack as an apron while working. Swelling of the genitals, a cardinal point in dermatitis due to underwear shorts, was absent in my patient.

Lichen Planus. Presented by DR. MAURICE J. COSTELLO.

B. H., a woman aged 51, presented from Bellevue Hospital, had typical lesions of papular lichen planus in 1938 and 1939. They were seen in the infra-

mammary regions, on the flexor surfaces of the wrists and on the inner aspects of the thighs. They disappeared when she was given weekly injections of mercury salicylarsenate.

Lichen Planus with Macular Atrophy (Schweninger-Buzzi). Presented by Dr. Maurice J. Costello.

I. H., a girl aged 20, daughter of the previous patient, presented from Bellevue Hospital, has had a papular type of lichen planus for the past four months involving the abdomen, the flexor aspect of the forearms and the inner aspect of the thighs. She also has an entirely different dermatosis which has been present since she was 5 years old. It consists of saclike, skin-colored, atrophic elevations, half the size of a pea, which herniate on digital palpation. They are discrete and are seen principally on the torso.

Lichen Planus Atrophicus. Presented by Dr. Maurice J. Costello.

E. H., a girl aged 12 years, sister of the previous patient, presented from Bellevue Hospital, was previously presented before the Metropolitan Dermatologic Society (Arch. Dermat. & Syph. **43**:737 [April] 1941). She had had this eruption for the previous nine months. It was located on the forehead, sides of the face, arms, forearms, thighs and legs. When she was admitted to the hospital, the eruption consisted of annular violaceous lesions, varying in size from that of a lentil to half that of a dime. The borders of the lesions were slightly raised and threadlike, with pale, pigmented atrophic centers. The lesions on the extremities were typical discrete pruritic lesions of lichen planus.

Treatment consisted of intramuscular injections of 1 cc. of bismuth subsalicylate (0.1 Gm. of bismuth subsalicylate) at weekly intervals. At this presentation, the lesions have undergone almost complete involution; pigmentation and atrophy replace the aforementioned lesions.

Carotenosis Cutis. Presented by Dr. Isadore Rosen.

W. M., a man aged 47 came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 13, 1940, complaining of an eczematous eruption on the hands. It was then noticed that the patient had a peculiar yellow discoloration of the face and other locations, which according to his statement had been present for about one year. The yellowish discoloration was visible particularly on the palms, soft palate and soles.

The patient gave a history of catarrhal jaundice for which he had been hospitalized at Bellevue Hospital in March and April of 1939. The icterus index was 150. Roentgenograms of the chest and of the gastrointestinal tract were normal.

The patient states that he has been eating raw carrots for years and that during the past year he has eaten two bunches of carrots a week. Laboratory examination showed the following results: An icterus index was 8.8 on one occasion and 14.2 another time. The result of a direct van den Bergh test was negative, and the bilirubin amounted to less than 1 unit. The urine was normal. The total yellow color amounted to 12.5 units, as determined by the icterus index. Of this 9.4 units was due to carotene and 3.1 units to bilirubin. Of the total carotenoid pigments, 0.47 mg. per hundred cubic centimeters was xanthophyll.

Poikiloderma Atrophicans Vasculare. Presented by Dr. David Bloom.

E. C., a woman aged 30, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 6, 1941 for treatment of an eruption which had started ten years previously in both axillary regions and had gradually involved the neck, cubital fossae, wrists, inner aspect of the feet and inner and anterior surfaces of the thighs.

The eruption surrounds each axilla in the form of an arch which extends from the lateral aspect of the chest near the axilla upward and then downward toward the inner aspect of the arm. The eruption consists of erythematous pinhead-sized and larger points (which cannot be made to disappear by pressure) and of depigmented and pigmented spots and slight scaling—a picture resembling radiodermatitis. The wrists and the inner aspects of the feet show similar but less pronounced plaques, and the cubital fossae, neck and inner and anterior aspects of the thighs show the same lesions still less pronounced. The lesions do not cause any subjective symptoms.

The Wassermann reaction of the blood was negative. The urine, a complete blood count and a differential count were normal. Microscopic examination of tissue from the axillas showed "possible reticuloendotheliosis."

DISCUSSION

DR. FRED WISE: I agree with the diagnosis. The loss of elastic tissue might be observed after a lapse of time, and it might be retained in the early stages of the dermatosis.

DR. WILBERT SACHS: It is peculiar that recently there have been many cases in which the clinical picture was that of poikiloderma and microscopically there was seen a reticuloendothelial process. Later, in several the condition has become straightforward clinical mycosis fungoides. In this slide there was no loss of elastic tissue, which one would expect in poikiloderma, although clinically the condition looks like poikiloderma.

DR. SAMUEL PECK: I have been studying for some time the effects of various injuries on elastic tissue. Usually the elastica is the first to be affected by inflammatory processes. The regeneration is slow and sometimes takes years. In any process of inflammatory and toxic nature, if the elastic tissue should not be involved it serves as an important differential diagnostic point. I would expect the elastic tissue to be greatly affected in this case. Clinically, however, I do not believe the condition is poikiloderma.

Lupus Vulgaris (Contracted from Mother, Who had Pulmonary Tuberculosis). Presented by DR. MAURICE J. COSTELLO.

C. T., a woman aged 50, had this lesion on the right side of her forehead for forty-five years. It measures about 2 by ¾ inches (5 by 1.9 cm.). It is solid, elevated, dusky red, slightly scaly and sharply demarcated. Medial to the principal lesion there is a pea-sized satellite nodule in which apple jelly nodules can be seen on diascopic pressure.

The patient's father died of rheumatic heart disease at the age of 27. Her mother died when the patient was 11 years old. She states that her mother had been suffering for several years from a pulmonary condition and that she was thin and emaciated. A short time before her mother's death the patient fell and sustained an injury at the site of the present lesion. The mother dressed the wound daily.

She has a sister 53 years of age, in good health.

DISCUSSION

DR. MAURICE J. COSTELLO: This patient is presented because I believe that at the time of her injury her mother, probably suffering from active pulmonary tuberculosis, was the contact.

Scrofuloderma Secondary to Osseous Tuberculosis (Probably Contracted from a Brother Suffering from Pulmonary Tuberculosis). Presented by DR. MAURICE J. COSTELLO.

V. B., a girl aged 14, presented from Bellevue Hospital, stated that she fell and struck her left knee when she was 6 years of age. Her knee became

swollen and painful. Six months later a diagnosis of tuberculous osteomyelitis was made by roentgen ray examination. Since that time she has had several operations, including fixation of the knee joint. In addition she has had rest in bed from 1933 to the present.

She presents on the posterior aspect of the left knee joint a nickel-sized ulcer with an elevated, irregular, rounded border and a granulomatous base covered with a seropurulent exudate. When this lesion was probed it was found to not communicate with the knee joint; her orthopedist stated that the bone has healed.

The patient's father, mother and older sister are living and well. A brother 34 years of age suffered from pulmonary tuberculosis during her childhood.

DISCUSSION

DR. MAURICE J. COSTELLO: This patient shows scrofuloderma which arose from an underlying focus of tuberculosis of bone. The main reason for presenting her is that the disease of the bone was probably contracted from a brother suffering from pulmonary tuberculosis.

Hairy Tongue. Presented by DR. E. WILLIAM ABRAMOWITZ.

H. F., a man aged 23, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 31, 1941 with a lesion on the tongue of five months' duration. It extends from 1 inch (2.5 cm.) from the tip posteriorly to the base. It is 1½ inches (4 cm.) wide, brownish and made up of threads. The patient has no subjective symptoms.

Microscopic examination revealed an acanthotic epidermis with no inflammatory process underneath (type of epidermis seen in a nevus).

Mycologic examination gave negative results.

Papilloma with Nevoid Epidermis Simulating a Supernumerary Mamma. Presented by DR. PAUL E. BECHET.

D. K., a man aged 39, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 27, 1941. He stated that ten years previously a soft noninflammatory pea-sized growth was removed from his left thigh by means of electrodesiccation, leaving a brown spot. Two years later the growth recurred, and for the last eight years it has grown slowly but steadily larger.

On the inner surface of the left thigh, 3 inches (7.5 cm.) below the groin, is a 2 by 3 inch (5 by 8 cm.) soft elevated tumor. The skin over the tumor is normal in color and noninflammatory. In the center of this soft breastlike growth is a dime-sized, brownish red, elevated, nipple-like area, which on light pressure with the finger feels herniated. On palpation the entire growth feels soft, blending with the surrounding areas. There are a few split pea–sized soft growths of light to dark brown distributed irregularly on the trunk.

The clinical picture is typical of lipoma which because of the nipple-like central areola strikingly simulates an accessory mammary gland, but the histologic diagnosis is papilloma with nevoid epidermis.

DISCUSSION

DR. WILBERT SACHS: A papilloma is a tumor of the papillae, and the term is commonly misused. The only lesions that approach this diagnosis are the small tabs that are frequently seen about the neck. I made a clinical diagnosis of lipoma, but the microscopic picture did not corroborate this. The section showed a nevoid epidermis, no hyperplasia of tissue and no fat. There was no glandular structure. It did not look like nipple tissue. I believe the condition is a nevus and not a neoplasm in the sense of being a lipoma.

DR. DAVID BLOOM: On clinical grounds I should say that the tumor consists of breast tissue, at least glandular tissue. A specimen for biopsy from the deeper tissue would enlighten one with certainty about the correct diagnosis.

DR. PAUL E. BECHET: The patient again presents the, unfortunately, too frequent conflict which occurs between clinical and histologic evidence. There is a definite clinical picture of a lipoma which, because of its conformation and the brownish central areola-like elevated patch, greatly simulates an accessory breast. The histologic report is that of a papilloma with nevoid epidermis, with nothing whatever characteristic of lipoma. This conflict in my opinion is more apparent than real and is greatly due to the lack of cooperation between the histologist and the clinician. The biopsy specimen was taken from the central pigmented nipple-like area and illustrates my contention, for clinically this central patch suggested some nevoid growth. Had a specimen been taken also from the tumor itself, I feel sure that the histologic structure of lipoma would have been demonstrated.

METROPOLITAN DERMATOLOGICAL SOCIETY

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Feb. 17, 1941

A Case for Diagnosis (Prurigo Nodularis?). Presented by DR. LESLIE P. BARKER.

M. H., a white woman aged 54, presents a lesion which began three years ago as a small nodule on the left leg just above the ankle. It started to enlarge two years later and within a few months attained its present size. Itching has been severe since the onset.

The patient has had varicose veins since the age of 15 and several attacks of phlebitis. The last attack, following a pelvic operation fifteen months ago, involved the right leg.

On the inner side of the left leg, just above the ankle, there is a circumscribed, silver dollar–sized, lichenified, bluish red, slightly roughened, scaly lesion with two excoriations over the surface.

Treatment has consisted of roentgen therapy, seven exposures of 100 r each. Locally she has used various antipruritic ointments. She has been given injections of estrone (theelin) and of liver extract, as well as liver extract by mouth.

The lesion became exudative after the application of 40 per cent salicylic acid several months ago.

The histologic picture was consistent with a diagnosis of prurigo nodularis.

DISCUSSION

DR. MAURICE J. COSTELLO: The area of the affected leg is a common site for varicose eczema. I suggest filtered roentgen ray therapy with a 3 mm. aluminum filter. This type of lesion is difficult to heal unless the patient remains in bed. A diagnosis of hypertrophic lichen planus should be entertained, which is much more resistant to therapy than lichenified eczema.

DR. LAIRD S. VAN DYCK: Hypertrophic lichen planus would be my diagnosis. Resistance to therapy of this dermatosis is the rule. I suggest giving the patient a series of injections of mercury salicylarsenate intramuscularly at weekly intervals.

DR. JOSEPH C. AMERSBACH: As Dr. Van Dyck has suggested, I would think of hypertrophic lichen planus and also of amyloidosis. In the cases that have come under my observation similar to the one presented, the congo red stain for

amyloid was positive. Filtered roentgen rays were given with good results. The lesions cleared up and remained well for a year or more and then recurred.

Dr. Henry D. Niles: The lesion is certainly atypical—which is one of the reasons why this patient was presented—and in such a case I think one must always consider an artefact. The lesion is surprisingly round and much more sharply circumscribed than those found in lichen simplex circumscriptus. I do not see any resemblance to lichen planus, but it might be a chronic lichenified eczema. A lesion is not necessarily hypertropic lichen planus just because it is resistant to therapy. If there were not enough changes in the histologic picture to make some other definite diagnosis, one would have to consider an artefact. I suggest that the lesion be covered with an occlusive dressing.

Dr. Royal M. Montgomery: The only additional idea I have to add is to suggest the diagnosis of hyperkeratotic psoriasis.

Dr. Thomas N. Graham: I think that the condition in this case is a lichenified eczema. It does not impress me clinically as being either hypertrophic lichen planus or psoriasis. These conditions would show some characteristic histologic features.

Dr. Leslie P. Barker: When first seen, this lesion resembled prurigo nodularis much more than it does now. The surface was dry, slightly scaly, raised above the surrounding skin and bluish red. At that time I entertained the diagnosis of prurigo nodularis or hypertrophic lichen planus. The itching has always been severe. The roentgen rays which she received were unfiltered except for 200 r, which were filtered through 1 mm. of aluminum. I applied an occlusive dressing to the lesion, but there was no improvement. The most improvement occurred immediately after the biopsy was performed.

Vesicular Eczema. Presented by Dr. Henry D. Niles.

J. B., a white man aged 30, born in the United States, was first seen in the dermatologic clinic of the New York Hospital on Oct. 23, 1940. At that time there were two round, circumscribed, red, crusted, oozing, vesicular, eczematous patches, the size of a dime, and a few discrete vesicles of seven months' duration on the back of his right leg, a small similar patch on the outer side of his left foot and two discrete vesicles on his left arm.

Microscopic examination and culture of material from these lesions showed no fungi. A trichophytin test elicited a 2 plus reaction in forty-eight hours, and a vesicular eczematous patch developed at the site of the reaction and persisted for several weeks. There was no eruption on his feet. He said that there were no allergic diseases in his family but that he had had hay fever for the previous five years. He had had no exposure to cats or dogs. He said that the patches had disappeared after the use of a gentian violet solution but had recurred one month before he attended the clinic and no longer responded to previous therapy.

He was given zinc oxide ointment with 5 per cent juniper tar and 1 per cent phenol, in addition to roentgen ray therapy (75 r), unfiltered, three times at intervals of one week. On December 4 the medication was changed to ointment of coal tar N. F. The lesions on his leg almost completely disappeared, but new similar lesions continued to develop on his arms and on the dorsa of his hands. Examination of these lesions also showed no fungi. The patient stated that he had not ingested any drugs. He presented no neurologic symptoms. The nose and throat were entirely normal. The uric acid content of the blood was 3.5 mg. per hundred cubic centimeters.

On December 23 sulfanilamide, 5 grains (0.3 Gm.), four times a day, was prescribed, and he has taken this regularly up to the present. Three weeks ago bacteriologic examination of material from one of the patches on the hands showed only hemolytic Staphylococcus aureus. Since then he has applied a 10 per cent ammoniated mercury ointment to all the patches except for one control patch on the left hand. All patches except the last-mentioned one have greatly improved with this ointment. The patient feels well, and he has no obvious foci of infection.

DISCUSSION

DR. RICHARD J. KELLY: Since the result of the trichophytin test was not conclusive and the results of the microscopic and cultural tests were negative, I think this eruption is an allergic eczema rather than just a yeast infection of the skin. I do not think the trichophytin test has much significance in this case.

DR. ROYAL M. MONTGOMERY: I think this condition fits the description of the disease called nummular eczema. I do not think it is an allergic eczema, and certainly it is not caused by his occupation. It is unusual that the patient has an eczematous reaction to trichophytin and not to oidiomycin or the control substance. I have had success by swabbing the lesions with 10 or 20 per cent silver nitrate.

DR. LESLIE P. BARKER: I believe this eruption may be due to a staphylococcic focus of infection elsewhere in the body. It certainly resembles eczematoid dermatitis, and I think the patient should be thoroughly examined for foci of infection. I doubt if much emphasis can be placed on the trichophytin test. I suggest trying sulfur and paste of zinc oxide N. F. locally. Of course, this will not eradicate the cause.

DR. MAURICE J. COSTELLO: I encounter cases of this kind from time to time, and they always present the same difficult therapeutic problem. I consider this eruption to be vesicular eczema with secondary infection. The improvement of the lesions by the local application of an antiseptic ointment and the lack of response to sulfanilamide therapy emphasize the importance of superimposed infection in the causation of this resistant eruption.

DR. LAIRD S. VAN DYCK: For lack of a better explanation of the cause of nummular eczema, I usually fall back on the hypothesis that it is due to a focus of infection. One may or may not be able to find such a focus in this case. The groups of vesicles also have a striking resemblance to herpes, which makes me wonder whether a virus could be responsible for some of the manifestations of the disease.

DR. JOSEPH C. AMERSBACH: I think this case is the type in which it is difficult to determine whether an allergy or changes in the weather are responsible. I believe it likely, from observation of a number of similar cases, that this patient's eruption will clear up in the spring.

DR. THOMAS N. GRAHAM: I believe the occurrence of the lesions only on the extremities is against the cause being a bacterial focus of infection. The fact that the eruption is definitely seasonal is also in favor of its being of external rather than of internal origin.

DR. HENRY D. NILES: The striking feature of this eruption is that it looks like a fungous infection but fungi are never found in the lesions. I think the reaction to trichophytin in this case is not significant. I do not consider that these eruptions are of occupational origin. There are discrete, circumscribed patches and never a diffuse dermatitis. I believe the lesions in cases of this kind are of systemic origin. The fact that they are limited to the extremities is no objection to this conception. The pustular bacterids described by Andrews are only on the palms and soles, but they are considered to be of systemic origin, as well as lupus erythematosus, which is usually limited to the center of the face. Most patients with this form of vesicular eczema say the lesions appear first in one place and then in another symmetrically in showers, as though due to dissemination of bacteria or fungi through the blood stream. I was intrigued by the idea that they might be caused by a virus, and I had Dr. Frank, who for some time has been studying virus diseases, study these cases, but he never found any evidence that the condition was due to a virus.

Morphea of the Penis. Presented by DR. LESLIE P. BARKER and DR. GERALD F. MACHACEK.

H. P., a white man aged 25, presents a painless small grayish smooth plaque of seven years' duration on the glans penis. The lesion has progressed

slowly. There was no preceding lesion, except perhaps a "bite" in this location. The lesion has been asymptomatic. There has been no urinary disturbance, and there is no history of venereal disease.

Examination reveals an irregularly shaped lesion, 2 cm. in diameter, on the ventrolateral surface of the glans penis, extending proximally to involve about 3 mm. of the prepuce. It is grayish white, flat topped, smooth and shiny. There is no induration or inflammation of the surrounding skin. A specimen has been taken for biopsy, but microscopic sections have not yet been completed.

DISCUSSION

DR. HENRY D. NILES: This case is extremely interesting. Presuming that there are no lesions elsewhere, the conditions which one would have to consider are morphea, atrophic lichen planus and lichen sclerosus et atrophicus. The last disease has been described as occurring on the penis and there is a picture of this in a recent article (Montgomery, H., and Hill, W. R.: Lichen Sclerosus et Atrophicus, ARCH. DERMAT. & SYPH. **42**:755 [Nov.] 1940). I suggest this diagnosis in spite of the fact that this lesion has no keratotic plugs. A histologic examination is necessary to make a definite diagnosis.

DR. JOSEPH C. AMERSBACH: I should like to see a report of a pathologic specimen before venturing a diagnosis in this case.

DR. MAURICE J. COSTELLO: I have never seen lichen sclerosus et atrophicus occur on the penis. The lesion this patient presents resembles that condition clinically, and I think that probably is the diagnosis. There are several half-dime-sized deep blue pigmented areas on a herniotomy scar in the right inguinal region at the sites of sutures. I believe that these are the result of a dye.

DR. RICHARD J. KELLY: When I first saw the patient I thought of lichen planus atrophicus. The patient had no other lesions of the mucous membranes, and I should be interested in seeing a report of the biopsy. There is a definite history of pigmentation along the herniotomy scar. It occurred after the operation and the sutures.

DR. LESLIE P. BARKER: This case was presented because of the fact that there was a single lesion limited mainly to the glans penis extending proximally to involve the skin of the prepuce. The biopsy specimen was taken from the cutaneous surface.

NOTE.—The subsequent report of the histologic examination was as follows: A section of the skin taken from the sulcus of the penis showed epithelium which had undergone hyperkeratosis and atrophy. A narrow zone of corium beneath the epidermal layer showed evidence of degeneration. It was eosinophilic and glassy but contained fine fibrils, and a relative acellularity was noted with scattered dilated capillaries within the degenerated areas. The deeper vessels were thickened with mural hyalinization. A band of mononuclear infiltration was seen just beneath the sclerosed cutis. The epidermis had partly separated from the corium. This cleft contained a few mononuclear leukocytes and chromatophores. The lesion was definitely lichen sclerosus et atrophicus.

The lesion of the abdominal wall was evidently a scar following herniorrhaphy, and within this area were embedded fragments of a foreign body, probably chromic catgut.

Solid Edema of the Ears Improved with Sulfanilamide. Presented by DR. MAURICE J. COSTELLO.

J. C., a white man aged 49, from Bellevue Hospital, had oozing and burning of the external auditory canals about six years ago, for which he applied "mint ice." About one and one-half years ago he noted a gradual onset of swelling of both ears. Sixteen months ago he was operated on for a carbuncle behind and below the right ear, and subsequently the solid edema of the right ear became

reduced. One month later, however, the swelling recurred and has persisted to date with an exacerbation about two weeks prior to admission to the hospital. Three years ago he had erysipelas of the left cheek. The right ear was more than twice its normal size. The normal markings were completely obliterated. The entire ear was dusky red, tense and edematous. There was slight crusting of the narrowed external auditory canal. The left ear presented a similar but less severe appearance. There is a healed X incision behind and below the right ear. On admission he was given sulfanilamide, 10 grains (0.65 Gm.) four times daily, and now states that his ears are much better than they have been for a year and a half.

DISCUSSION

DR. RICHARD J. KELLY: The only similar treatment that I have seen has been in the cases of solid edema of the upper lip. At the Vanderbilt Clinic I have treated patients over a period of five years with sulfanilamide, and they have responded well. Others have responded to erysipelas toxin. I wonder whether Dr. Costello has had cultures of any foci of infection.

DR. ROYAL M. MONTGOMERY: About two years ago I encountered a similar case in which the condition was limited to the left ear. The patient had had much therapy in different parts of the country with little improvement. He had an intensive course of sulfanilamide with little therapeutic result. The sulfanilamide definitely seems to have improved the condition in Dr. Costello's case.

DR. ANTHONY C. CIPOLLARO: The therapeutic result in this case is excellent. When sulfanilamide, sulfapyridine or sulfathiazole is used for any condition, it should be administered in sufficiently large doses to yield good therapeutic results. Small doses are apt to make the patient resistant to therapy. When indicated and when there are no untoward symptoms, 45 grains (3 Gm.) a day should be administered. However, I have seen good results with small doses in a few cases.

DR. LAIRD S. VAN DYCK: I think the therapeutic result is splendid in a stubborn condition. If it is due to a focus of infection, perhaps it will recur when administration of the drug is stopped. I have observed 2 or 3 cases of solid edema of the upper lip. In 1 case the condition improved after ammoniated mercury ointment was applied to the nasal mucosa, where a folliculitis involving the vibrissae had been found.

DR. MAURICE J. COSTELLO: I thought, before I sent this patient to the hospital from the outpatient department, that I was going to get this good result, since I have had similar improvement in this condition several times. Solid edema may follow the irritation and infection caused by removing ear wax with a hairpin or similar instrument. I recall one patient who was sent to a hospital for contagious diseases every time she had an exacerbation of this type of erysipelatous eruption accompanied by slight fever. I think the foci of infection are in the external auditory canals. Sulfanilamide can be given in relatively large doses for long periods provided the person is not suffering from an acute disease with constitutional reaction. For the treatment of chancroid, for instance, I administer 120 grains (8 Gm.) on the first day, 80 grains (5.2 Gm.) on the second, 60 grains (4 Gm.) on the third and 40 grains (2.6 Gm.) a day for a long period, at times about six weeks. I think that sulfanilamide should be tried in all cases of solid edema or chronic lymph stasis secondary to streptococcic infection.

Granuloma Inguinale with Spontaneous Amputation of the Penis. Presented by DR. MAURICE J. COSTELLO.

J. W., a Negro aged 38, from Bellevue Hospital, had a painless "sore" on the foreskin in 1932, which within one year resulted in paraphimosis for which circumcision was performed. This resulted in ulceration of the line of incision,

which gradually spread peripherally and healed centrally. In 1935 a plastic operation was performed on the glans penis, but the ulceration persisted. He has been treated in four different hospitals during this time. He was given injections in the arm, about one hundred of them, in Bridgewater State Hospital, with no improvement. The lesion gradually caused erosion of the entire penis and swelling of the scrotum.

On admission the penis was completely destroyed. There was a granulating ulceration of the scrotum and crural regions with a central clean papillomatous area and a raised, grayish, firm border. Several circumscribed smaller eroded areas with granulating centers and raised grayish borders were also present. The scrotum was about four times its normal size.

The Wassermann reaction of the blood was negative. The intradermal test with Frei antigen and with Ducrey vaccine elicited negative reactions. Donovan bodies were found in smears of material from the lesion.

Since his admission to Bellevue Hospital the patient has been given fuadin three times weekly with immediate good results. He has had a total of fourteen injections to date, 5 cc. three times a week.

DISCUSSION

Dr. Franklin H. Grauer: This case is a classic one of granuloma inguinale. It exhibits strikingly the tendency for this condition to spare the regional lymph nodes. Although this patient's genitalia have been practically entirely destroyed by the process, the satellite lymph nodes appear clinically uninvolved. It is gratifying to know that injections of fuadin will often be efficacious in this condition when antimony and potassium tartrate fails.

Dr. Leslie P. Barker: I doubt if one can consider four years' quiescence a cure for granuloma inguinale. There are several different drugs on the order of antimony and potassium tartrate which will clear these lesions for a time; tometimes one will do it and sometimes another. I had a case at City Hospital of extensive granuloma inguinale of both labia in a young Negress, who remained free for three or four years after surgical amputation of both labia and then had a recurrence.

Dr. Henry D. Niles: Recently I read a report on the use of sulfanilamide in the treatment of granuloma inguinale. According to this report the results were satisfactory, although I had previously believed that this condition was one which was not helped by sulfanilamide.

Dr. Laird S. Van Dyck: It is interesting to me that one antimony compound (fuadin) should have proved to be so much more effective than another (antimony and potassium tartrate).

Dr. George Morris (by invitation): At Bellevue Hospital there were about 15 patients in the past year with granuloma annulare in whose lesions Donovan bodies were found. Antimony and potassium tartrate is not as effective as fuadin in the treatment of this disease. If the condition does not respond to fuadin, it will not respond to the other compound either. It is agreed, certainly, that if this man were discharged now he would have a prompt recurrence, but if fuadin treatment is continued for six or eight months he will be cured. I have treated mixed infections of granuloma inguinale and chancroid with sulfanilamide; the latter responds well, but the former is unaffected by this therapy.

Finding Donovan bodies is relatively easy. There are a few tricks in doing it. I think, in the first place, in making a smear for Donovan bodies one must take a biopsy specimen from the periphery of the lesion; wipe the blood off the specimen, leaving just a little blood and tissue. It must be stained thoroughly, even a little overstained. The slide should be examined with low power magnification at the periphery of the smear. One will find Donovan bodies in the third or fourth smear if they are present.

The new five day intensive treatment with mapharsen will not cure granuloma inguinale when it occurs coincidentally with early syphilis. Donovan bodies have been found at the end of this intensive antisyphilitic therapy. In the lesions of a man with a mixed infection of chancre and granuloma inguinale Donovan bodies were found after the five day treatment.

DR. MAURICE J. COSTELLO: I agree with everything that Dr. Morris has said, because that has been my experience at Bellevue Hospital, where there are always a number of patients suffering with this disease. I agree that fuadin is a superior drug to antimony and potassium tartrate, or at least that it is often effective when the latter fails. Treatment should be continued for months after there is no clinical evidence of the disease; early withdrawal of the drug is the cause of many recurrences. I have seen the same type of destruction of the penis from chancroid. Sulfanilamide appears to be of no value in the treatment of granuloma inguinale.

Ulcerative Lymphadenitis in a Patient with Tertiary Syphilis. Presented by DR. MAURICE J. COSTELLO.

M. G., a Negress aged 43, from Misericordia Hospital, has had a torpid inflammatory swelling of the epitrochlear, left preauricular and right posterior cervical lymphatic glands with ulceration of the overlying skin for the past six weeks. A Wassermann reaction of the blood was positive (4 plus). An intradermal test with Frei mouse brain antigen elicited a positive reaction. The result of an inverted Frei test was negative. Inoculation of guinea pigs with the macerated lymph gland did not show tuberculosis. The histologic structure of one of the excised lymphatic glands revealed tertiary syphilis. The lesions underwent prompt involution after treatment with mapharsen and bismuth subsalicylate.

DISCUSSION

DR. FRANKLIN H. GRAUER: This case is interesting. I suggest staining the pus from the draining lymph nodes for tubercle bacilli and obtaining a culture. I think a biopsy should be performed. The patient also should have a complete physical examination and a roentgenogram of the chest. It is difficult to make a diagnosis in this case on physical changes only. I believe one can exclude the deep mycotic infections, and I do not think that syphilis is producing this clinical picture, in spite of the positive Wassermann reaction. It is known that gummatous adenitis occurs, although I believe it is relatively rare. A multiple, symmetric, fluctuant gummatous adenitis with draining sinuses would seem to me an even rarer occurrence. Taking all the data at hand into consideration, I favor the diagnosis of tuberculosis of the lymph nodes.

DR. RICHARD J. KELLY: I agree with everything that Dr. Grauer said.

DR. HENRY D. NILES: This condition is most difficult to diagnose. One must seriously consider tuberculosis and also a deep fungous infection, such as sporotrichosis or actinomycosis. I recently observed a case of proved sporotrichosis in which there were three lesions on the arm, only two of which were in linear arrangement, and a lesion on the forehead, which is most unusual. The patient just presented has a deep ulcerated lesion on one arm which strongly suggests sporotrichosis. In this case one must also consider actinomycosis, tuberculosis and possibly syphilis.

DR. JOSEPH C. AMERSBACH: I agree with Dr. Grauer that the results of the serologic tests probably mean nothing in this condition. It is fairly well known that a patient may have a false positive reaction, which undoubtedly occurred in this case. I favor a diagnosis of tuberculosis.

DR. ROYAL M. MONTGOMERY: I favor a diagnosis of tuberculosis. I do not think the condition is sporotrichosis because of the symmetry of the large soft nodules in the lymphatic areas.

DR. ANTHONY C. CIPOLLARO: I do not think that one can make an unequivocal clinical diagnosis in this case. There are characteristics which fit in with tuberculosis, with sporotrichosis, with actinomycosis and with syphilis. A biopsy and an examination of the pus for fungi and bacteria are essential. If I were forced to confine myself to one diagnosis, I would favor syphilis.

DR. LAIRD S. VAN DYCK: If I were forced to make a diagnosis, I would favor tuberculosis, until further observation sheds more light on this case. The lesions are widely scattered and resemble lymph nodes undergoing necrosis and ulceration.

DR. MAURICE J. COSTELLO: When I saw the patient a week ago in the clinic, I made the diagnosis of tertiary syphilis, bilateral symmetric gummatous lymphadenitis. When the Wassermann reaction of the blood was reported as 4 plus, I felt that this confirmed my clinical impression. The lesion began as inflammatory nodes which broke down and discharged a serosanguineous material. I do not think that tuberculous lymphadenitis would present this picture. Tuberculous lymphadenitis is usually accompanied by pain and varying degrees of inflammation. The duration, distribution and behavior of this condition and the age of the patient are not in favor of that diagnosis.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *President*

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March 25, 1941

Linear Nevus with Intense Pruritus. Presented by DR. J. GARDNER HOPKINS.

J. B., a boy aged 2½ years, showed at birth a red mark extending down the inner side of the thigh and the lower portion of the leg. During his first year the infant began to scratch this lesion. He has since complained of intense, almost continuous itching and of pain when the lesion was dressed or handled. There were frequent paroxysms of crying day and night. When he was first seen, a year ago, there were exuding and crusted lesions in a band from Poupart's ligament to the internal malleolus. Cultures showed Staphylococcus aureus only. Under mild antisepsis the lesions became dry and presented a lichenified appearance typical of a linear epidermal nevus. The pruritus continued to be severe until four roentgen ray treatments of 100 r each were given three months ago.

The case is presented as an instance of pruritus due to a linear nevus or to infection localized in a linear nevus.

DISCUSSION

DR. HOWARD FOX: This lesion is a so-called linear nevus, though much of the lesion has the form of a broad band. This condition, which is clinically and histologically a nevus, in some cases causes intense itching for some unknown reason.

DR. FRANK C. COMBES: I agree with the diagnosis of linear nevus which is intensely pruritic. I think this condition is particularly resistant to radiotherapy. It may be relieved temporarily, but gradual progressive destruction is the only way in which one can eliminate the lesions.

DR. R. H. RULISON: I was interested in this case because I presented a case of unilateral pruritus with linear nevus three months ago (ARCH. DERMAT. & SYPH. **44**:101 [July] 1941). There was itching in the areas involved by the nevus. I did not realize that itching was a common feature of linear nevus. I should be glad to know in what percentage of cases of linear nevus there is itching.

DR. FRED WISE: I agree with Dr. Fox. In my experience nearly all verrucous linear nevi are associated with itching. I believe this form of nevus to be incurable with ordinary methods of treatment. One must resort to surgical removal and plastic procedures. I think electrodesiccation would cure this lesion but with scar formation.

DR. J. GARDNER HOPKINS: Dr. Fox and Dr. Wise brought out a point on which I wanted information, namely, whether pruritus was common in these lesions and whether the lesion was the probable explanation for the pruritus.

DR. EUGENE F. TRAUB: Is the lesion spreading?

DR. J. GARDNER HOPKINS: I do not think so.

DR. EUGENE F. TRAUB: This type of nevus is apt to develop slowly in progressive stages or steps. I have under observation a woman in the forties who has a linear nevus which even at present is extending. Therefore, if the lesion is excised, one is apt to find that new areas will develop beyond the area that has been removed. Of course, this would apply to any type of treatment that might be suggested, but I think that deep desiccation and curettement, or even deep freezing with solid carbon dioxide, are often preferable to surgical removal. Either the patient or the family, however, should be warned of the possibility of new lesions appearing, so that the treatment will not be blamed for them when they appear.

DR. HOWARD FOX: I do not agree with Dr. Wise that itching is a feature of the majority of linear nevi. If this were so, the fact would be mentioned in dermatologic textbooks. Severe itching is present in my experience in only a minority of the cases.

DR. GEORGE M. MACKEE: It has been my experience that electrodesiccation and electrocoagulation have not been effective. Recurrence is common. It is amazing how much destruction is necessary for a cure. If a verrucous nevus is of a size and location suitable for excision, this procedure is the method of election; otherwise, I favor a plastic operation. I agree with Dr. Fox about the frequency of pruritus.

Tuberous Sclerosis Associated with Adenoma Sebaceum, Epilepsy and Abnormal Mentality. Presented by DR. HOWARD FOX.

C. S., a girl aged 6½ years, is an only child born of American parents married four years. The parents gave no history of consanguinity, and no relative has suffered from a similar disease.

The patient has an abnormal personality; she suffers from epilepsy and presents various congenital abnormalities of the skin and of one eye. She is precocious, nervous and highstrung and, according to her mother, does not get along well with her schoolmates. She began to walk at the age of 13 months and to use words at 12 months. For several years she suffered from attacks of petit mal, becoming unconscious for several minutes but not biting her tongue or falling. She has been treated by sedatives during the past year, during which time the attacks of petit mal have not recurred.

The teeth, the nails and the hair of the scalp are normal. There is slight hypertrichosis of the face. The most noticeable cutaneous abnormality is a typical eruption of the Pringle type of adenoma sebaceum. This consists of a symmetric, fairly profuse eruption of the face, involving especially the cheeks, chin and nose. The lesions are red, discrete and semisolid and are mostly the size of a small pinhead. Many show telangiectases. On the left cheek and temple is a slightly elevated, infiltrated plaque which is faintly yellow. At the left angle of the jaw are flesh-colored warty masses from 5 to 15 mm. in diameter. Scattered over the neck, back, trunk and legs are a few small pigmented and hairy nevi. On the lower left quadrant of the abdomen there is an oval patch of complete depigmentation measuring 5 by 7 cm. In the sacral region there is an irregularly shaped, slightly verrucous and pigmented patch on which there is slight hypertrichosis.

The mucous membranes of the mouth are normal except for two yellowish white elevations the size of a pinhead under the tongue and adjacent to the sublingual duct. There are no subungual fibromas. A congenital defect in the right eye consists of a round whitish filmlike patch about 3 mm. in diameter. About two thirds of this patch covers the iris and one third the sclera. The vision is not affected.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis as presented. I should like to call attention to the fact that there is one feature lacking to make a complete picture, namely, subungual fibromas and warts, which are frequently associated with this syndrome.

Scrofuloderma. Tuberculosis Cutis. Presented by DR. EUGENE F. TRAUB.

M. H., a girl aged 14, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 14, 1941. There is no family history of tuberculosis. In June 1940 the patient noted an enlarged lymph node on the left side of the neck. In July a lesion developed near the inner canthus of the left eye which looked like a boil. This was incised first in July and several times after that, but it failed to heal. The lymph node in the neck was red and inflamed in September and was incised at that time.

The Wassermann reaction of the blood was negative. A patch test for tuberculosis was said to have elicited a positive reaction at another institution. Histologic examination showed tuberculosis, probably scrofuloderma. The question of a tuberculous dacryocystitis was to be settled by members of the ophthalmic department, where the patient was referred for examination of the eye.

Treatment has consisted of the exposure of two areas to ultraviolet radiation.

DISCUSSION

DR. FRANK C. COMBES: The patient has a scar on the neck over a lymph node, which I presume is the location of the scrofuloderma. I agree with the diagnosis on the basis of the history and the histologic changes. The lesion on the nose does not seem to be connected with the lacrimal gland but seems more superficial and too far forward to have any connection with the duct. It apparently moves freely with the skin. In view of the histologic changes I suggest the diagnosis of hypertrophic lupus vulgaris.

DR. HOWARD FOX: I should like to know if there is a fistula leading to the lacrimal duct.

DR. EUGENE F. TRAUB: This patient was referred to the ophthalmic department yesterday for consultation, but the report is not yet available. I am unable to answer the question.

DR. GEORGE C. ANDREWS: I favor the diagnosis of lupus tumidus with scrofuloderma in a tuberculous subject.

DR. GEORGE M. MACKEE: The case impresses me as one of hypertrophic lupus vulgaris. A scar would look much better than the granuloma. The lesion can be destroyed completely, I think, with curettage and electrodesiccation or electrocoagulation. It might also respond favorably to roentgen ray treatment in safe doses. In a girl of that age with a long expectancy of life I should hesitate to give erythema doses of roentgen rays because of the danger of sequelae ten years later, but I should not hesitate to give one or two suberythema doses at intervals of one month. In addition to local therapy, everything possible should be done for her general health, just as one would do for pulmonary tuberculosis. She should have a nourishing, high vitamin diet, rest, heliotherapy and so on. If the lesion responds favorably to roentgen rays, there will not be much of a scar. The bulk of the lesion may disappear, but some nodules will remain. These will have to be destroyed individually by some destructive method, such as electrosurgery.

DR. J. GARDNER HOPKINS: The lesion is unusually edematous in hypertrophic lupus vulgaris. I wonder if the history that the nodes preceded the ocular lesion for a long time is reliable and whether the remote possibility of tularemia should not be considered.

DR. HOWARD FOX: Tularemia can be excluded, I think, by the lack of conjunctivitis, which is one of the first signs of that disease, and by the duration of the lesion. I should like to ask whether Dr. MacKee referred to the formation of a cataract in warning against large doses of roentgen rays.

DR. GEORGE M. MACKEE: I did not mean cataract. I meant a prickle cell epithelioma, which would be worse than what she now has.

DR. EUGENE F. TRAUB: This patient was presented chiefly for suggestions as to treatment of the lesion of the inner canthus. I had in mind the possibility of excision, which seemed to me possibly the best method of treatment. I believe the lesion is probably best labeled tuberculosis cutis rather than lupus vulgaris, as it does not show apply jelly nodules. I have had only moderate success in the treatment of such lesions with roentgen rays, but perhaps I have not given large enough doses. Certainly some destructive method of treatment should be employed before the lesion has any chance to spread. I will check as to the possibility of tularemia. I did not think of that at all because the involvement of the node antedated that of the lesion of the eye and also because the histologic structure was that of tuberculosis.

DR. FRANK C. COMBES: I suggest that an opaque solution be injected into the lacrimal duct under pressure and that roentgenograms be made to see if there is any connection between the lacrimal sac or duct and this lesion. If not, I should prefer excision and plastic surgical repair to irradiation. I think that for a lesion as small as this one near the eye, better results are obtained with excision than with radiotherapy or galvanocautery.

Livedo Reticularis. Presented by DR. EUGENE F. TRAUB.

B. R., a boy aged 12 years, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 19, 1941, complaining of an eruption of one year's duration. There is a history of tuberculosis on the maternal side of his family. The patient complains of frequency of urination, which has been going on for a long time and has become worse in the past four or five months. For several months he has had abdominal cramps lasting ten to fifteen minutes, not relieved by voiding. There has been no vomiting and no pain in the back. Occasionally he is unable to hold his urine, while at other times there is difficulty in starting the stream. His mother feels that he drinks more water than the average child. His appetite is not particularly good, but there has been no loss of weight.

Physical examination in the medical department showed principally that the boy was of short stature and underweight, with macular-like lesions of the legs, possibly of vasomotor origin. The eruption consists of mottled areas of the skin, varying in size and in configuration and located on the face, on all the extremities, but most pronounced on the legs, and to a lesser extent on the body. The lesions are of a deep purple, which fades on pressure. The mother says that this condition began last winter and is worse in cold weather.

DISCUSSION

DR. FRED WISE: I believe that treatment with acetylbetamethylcholine (mecholyl) is effective. It is administered by iontophoresis.

DR. HOWARD FOX: I think that the eruption tends to become less evident or even to disappear when adult life is reached. I have not had the opportunity to follow a case of this kind for years, but the disease is undoubtedly less common in adults than in children.

DR. GEORGE C. ANDREWS: I have the impression that many cutaneous vascular disturbances like this one are associated with disorders of the pituitary gland. This child is short, and I think injections of an anterior pituitary extract containing the growth factor once a week for a few months might help. I should give a little thyroid along with it.

DR. EUGENE F. TRAUB: This boy was sent to the medical clinic for a special study of the circulation. No suggestions as to treatment were received.

Macular Atrophy with Pseudotumors of the Schweninger and Schweninger-Buzzi Type in a Negress. Presented by DR. J. GARDNER HOPKINS.

S. T., a Negress aged 31, is presented from Vanderbilt Clinic. Lesions first appeared on the neck and chest eighteen months ago. The patient now has pustular acne on the face and neck. Over the entire trunk are thickly scattered depigmented plaques measuring from 8 to 20 mm. in diameter. Some are groups of dilated follicles with a white ring about each. Others show flat wrinkled thinned skin. Others are raised and feel firm, although they can be pressed down to the level of the skin with a glass. There is no evident herniation of the skin. The patient shows typical striae atrophicae over the hips.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR. GEORGE C. ANDREWS: I agree with the diagnosis made by the presenter. Most of the lesions are in the edematous stage of the disease.

DR. FRANK C. COMBES: This case is almost identical with one I reported several years ago (ARCH. DERMAT. & SYPH. **22**:1022 [Dec.] 1930).

DR. HOWARD FOX: I agree with Dr. Combes.

DR. FRED WISE: I agree with the diagnosis as presented.

DR. GEORGE M. MACKEE: I agree with the diagnosis of idiopathic macular atrophy.

DR. EUGENE F. TRAUB: Is idiopathic macular atrophy the same as the Schweninger-Buzzi type, or is the Schweninger-Buzzi type a specific entity?

DR. J. GARDNER HOPKINS: I withdraw the diagnosis of Schweninger-Buzzi pseudotumors in view of the general opinion that the raised lesions represent the early edematous stage of macular atrophy.

Extensive Lupus Erythematosus in a Negro with Atrophy and Depigmentation. Presented by DR. A. BENSON CANNON.

C. N., a Negro aged 65, married, a longshoreman, born in North Carolina and a resident of New York city for twenty-one years, is presented from Vanderbilt Clinic complaining of an eruption of the scalp and face of six years' duration. He was first seen there on March 11, 1941. He has attended hospital clinics since January 1934 and has received many injections of gold sodium thiosulfate, bismuth and mercury, together with local therapy. The eruption began in January 1934 as a "pimple" on the left cheek below the eye which has since gradually spread. During the early stages this area was pruritic.

Examination shows on the right half of the scalp a depigmented area of alopecia, about 10 cm. in diameter, with an occasional tuft of gray hair in the center of an island of normal pigmentation. Fine vessels are present in the lesion along with atrophy. Several other similar but smaller affected areas are present on the scalp. Similar lesions are seen on the ears, the face and the nose, with a butterfly distribution on the chin and the forehead. The nose is completely involved from the tip to the glabella. The lobule of the right ear shows evidence of destruction. The edges of the lesions are irregular in outline and configuration and are more deeply pigmented than the normal skin. Some follicular plugging is readily seen on the cheeks. No other area of the body is involved, but the

glans penis has areas of depigmentation without other changes. General physical examination was otherwise normal except for hypertension. The blood pressure was 224 systolic and 120 diastolic, and there was some cardiac enlargement.

The Wassermann reaction of the blood was negative. Urinalysis showed a 1 plus reaction for albumin and 1 to 2 fine granular casts. A blood count showed 5,060,000 erythrocytes and 4,500 leukocytes, with 45 per cent polymorphonuclear leukocytes, 37 per cent lymphocytes and 16 per cent mononuclear leukocytes. There was 100 per cent hemoglobin. Histologic examination showed lupus erythematosus.

DISCUSSION

DR. J. GARDNER HOPKINS: I agree with the diagnosis as presented.

DR. R. H. RULISON: I agree with the diagnosis as presented.

DR. HOWARD FOX: In my experience, lupus erythematosus with striking depigmentation and atrophy is not a rarity in the Negro.

DR. EUGENE F. TRAUB: I should like to ask a question about Dr. Fox's statement that this condition is not so uncommon in the Negro. Does not severe lupus erythematosus in the Negro nearly always result in this depigmentation?

DR. HOWARD FOX: Yes.

DR. EUGENE F. TRAUB: Then it is fairly common to see this depigmentation in a Negro with lupus erythematosus. Is there any explanation for that?

A Case for Diagnosis (Neurodermatitis Circumscripta? Amyloidosis?).
Presented by DR. GEORGE M. MACKEE.

N. K., a man aged 23, originally registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 14, 1932 with cutaneous lesions of seven years' duration. At that time he presented severe pityriasis capitis, circumscribed areas on the left eyebrow covered with yellow crusts, moderate erythema of the forehead and about the eyes and areas of chronic lichenification in the left popliteal space and on the buttocks. He gave a history of having received twelve roentgen ray exposures to the left eyebrow, the last one a month prior to his registering at the clinic.

The patient was previously presented by Dr. Marion B. Sulzberger before the Section of Dermatology and Syphilis of the New York Academy of Medicine on April 6, 1937 for diagnosis (A Case for Diagnosis [Ulerythema Ophryogenes? Neurodermatitis Decalvans?] ARCH. DERMAT. & SYPH. **36**:1284 [Dec.] 1937).

On Feb. 15, 1941 the patient returned to the clinic after an absence of one year for a check-up, stating that there had not been any change in his condition. He has lately been in good health, except for an obstruction of the nose. He complains occasionally of absent-mindedness. He has never had any other cutaneous disturbance. On and off for ten years he suffered from "ulcers of the stomach," for which he was treated with dietary measures. In the past he had had scarlet fever, measles and pneumonia. The patient has six sisters and one brother, all in good health, none with a similar disturbance of the skin. A nephew has asthma, and his father has bronchial catarrh.

The skin has been rough and dry for many years, especially around the nates. Fifteen years ago a dime-sized nonpruritic scaly patch appeared on the glabella. It cleared up after treatment with a salve for four months and then recurred and spread slowly to the left eyebrow and forehead. It has never since regressed. In 1928 the hair of the eyebrows began to fall out. This alopecia spread to the left side of the face and chin, involving the right cheek in the last six years. The alopecia has been slowly progressive and permanent. In 1932 two to three small nodules appeared on the upper border of the present patch on the forehead, others gradually and very slowly developing and reaching the present distribution within six years. They have been stationary for the last three years. A few of the nodules on the upper margin seem to be getting smaller and softer, about one half their original size, while the others seem to be getting larger. They have never undergone involution. They are painless and not pruritic.

The patient is well developed, of average intelligence and about 5 feet 6 inches (168 cm.) in height, weighing about 175 pounds (79 Kg.) and appearing to be in good health. On the lower half of the forehead, including the glabella and the root of the nose, and extending laterally to the outer edges of the eyebrows, are discrete but grouped closely enough to give the semblance of a patch, match head–sized to lentil-sized, skin-colored, round, rather opaque, fairly soft nodules. There are similar growths scattered on both sides of the face and on the sides and front of the neck. All of the lesions, except for a few on the front of the neck, are easily compressible on diascopic pressure, leaving white, uniform spots. The skin, especially of the forehead, is thick, slightly erythematous, dry and rough. There is some alopecia of the right eyebrow and almost complete absence of hair on the left eyebrow and the entire face except for a fine border along the mandibles. There are several slightly raised brown nevi on the chin and sides of the face and also fairly numerous pinpoint-sized to match head–sized, cherry red, vascular nevi scattered on the trunk. There are moderate seborrhea and alopecia on the vertex of the scalp. There are large, fairly symmetric areas of alopecia on the inner surfaces and backs of the thighs and on the outer and posterior surfaces of the legs. There is an irregular, brownish, pigmented patch in the sacral region. The skin of the buttocks and thighs is slightly erythematous and, although not atrophic, appears to be thinner than usual. The skin of the lumbar and sacroiliac regions is white and presents at the level of the iliac crests a distinct line of demarcation from the darker skin above.

The sella turcica was small but within normal limits of size. The basal metabolic rate was —20 per cent. There was hypotension (blood pressure, 98 systolic and 60 diastolic). The urea concentration in the blood was 19 mg. per hundred cubic centimeters. All other routine and special laboratory tests, including tuberculin tests, cutaneous tests and examination of the blood for cholesterol and of the serum for calcium, gave normal results. Recent examinations included examination of the urine for hematoporphyrin, which revealed a normal value, determination of vitamin A concentration of the blood, a dark adaptation test, fluoroscopic and roentgenographic examinations of the chest and examination of the endocrine system.

Histologic examination of a nodule on the forehead on July 1, 1933 suggested lupus erythematosus in an early stage. The histologic examination of a similar nodule on Oct. 31, 1935 revealed nothing to justify a diagnosis. Two biopsies were performed on nodules on the forehead on March 18, 1941, and the histologic report by Dr. Sachs was as follows: "At the edge of the section was a dilated follicle the walls of which were acanthotic. About the follicle was a pronounced cellular infiltration composed chiefly of small round and wandering connective tissue cells. In the center of the section there was a large mass extending throughout the entire cutis. In this mass were numerous small dilated blood vessels. The matrix was loose and lacy about these vessels. There was a diffuse cellular infiltrate of round cells, wandering connective tissue cells and polymorphonuclear leukocytes. The elastic tissue did not show features of lupus erythematosus. There was no evidence of multiple benign cystic epitheliomas or of lupus erythematosus."

DISCUSSION

DR. FRED WISE: This patient has been under my personal observation for about six years, and I have been unable to come to any conclusion with respect to the diagnosis during that time.

DR. J. FRANK FRASER: My first impression was that the condition was adenomatosis of the sweat glands. However, that diagnosis can be excluded by the histologic picture.

DR. A. BENSON CANNON: I would consider the possibility of the lichenoid dermatitis being due to a retention of arsenic and suggest that a specimen of blood and one of urine be examined for arsenic.

DR. GEORGE M. MACKEE: I cannot explain the nodules on clinical or on histologic grounds. The case was considered by some observers for several years

to be one of ulerythema ophryogenes. I made a tentative diagnosis of neurodermatitis because it has some of the clinical features of that disease, but the patient claims that it does not itch. Also, if one can believe his statement, the loss of hair apparently is not due to rubbing, as it would be if the condition were neurodermatitis. I suspect it may be some form of lipoidosis. Further histologic study with special stains is required.

DR. FRED WISE: I should like to ask Dr. Cannon, since he has had a great deal of experience with the investigation of arsenical retention, whether it is possible for an arsenical dermatitis to cause an atrophy of the outer half of the eyebrows.

DR. A. BENSON CANNON: I think that arsenical dermatitis, or any other chronic eczematoid condition affecting the skin in and around the eyebrows, is apt to cause an alopecia. Chronic arsenical dermatitis may also produce atrophy of the skin. It might be of some diagnostic importance to compare the amount of arsenic found in the abnormal skin with that found in the normal; the affected parts usually contain more arsenic than the normal skin.

Keratosis Follicularis (Darier). Presented by DR. A. BENSON CANNON.

J. H., a man aged 52, is presented from the clinic of the New York City Hospital, Welfare Island, complaining of an eruption involving the scalp, face, trunk and upper extremities of ten years' duration. Ten years ago the patient went to a clinic for treatment of lesions on the forehead and chest. He was told that he had psoriasis and was treated with sulfur. The condition remained unchanged for ten years, until four months ago, when many new lesions appeared on the scalp, face, back and arms.

He was first seen at the clinic in January 1940, when a tentative diagnosis of seborrheic dermatitis was made and four fractional doses (75 r) of unfiltered roentgen rays were given. The character of the lesions changed; the waxy crusts disappeared, and a tentative diagnosis of Darier's disease was made. This was confirmed by histologic examination of a specimen taken from the back. His diet was found to be deficient in vitamins. He had been taking coffee and plain milk for breakfast; a sandwich (ham or cheese) or nothing for lunch; lamb stew, veal cutlet or corned beef, cabbage, string beans or carrots (only one at a time), coffee and stewed fruit or apple pie for dinner. He stated that he had not taken any laxative or pills for headache. He admitted taking rye whisky or beer every day, sometimes to excess.

Examination shows on the face, trunk, arms and scalp many pinhead-sized to split pea–sized, dark red to skin-colored, elevated, hard papules with a central keratotic plug. The lesions are grouped particularly over the ear and behind the ear lobes, on the central portion of the chest and in the center of the back. Numbers of the lesions are covered with a dirty gray crust. Other lesions are scattered over the scalp, arms and lower portion of the abdomen.

The urine and the blood count were normal. Histologic examination showed the typical picture of keratosis follicularis.

DISCUSSION

DR. J. FRANK FRASER: I should like to call attention to a series of cases reported by Drs. Kyrle and Pawloff (Kyrle, J.: *Arch. f. Dermat. u. Syph.* **123**:466, 1916; Pawloff, P. A.: *ibid.* **152**:34, 1926) in which the clinical picture closely resembled that of Darier's disease. They called the condition keratosis follicularis et parakeratosis follicularis in cutem penetrans. The differential diagnosis from Darier's disease was made on the basis of the histologic picture. In these cases the hyperkeratotic plugs penetrated the basal layer and extended into the corium. There was also a foreign body reaction in the corium and absence of *corps ronds* in the epidermis. I did not have the opportunity of seeing the slides in this case, but I suggest that if any of these features are present—features which are never observed in Darier's disease—the condition is not Darier's disease.

DR. FRANK C. COMBES: I agree that this patient presents some of the characteristics of Darier's disease, but the absence of any familial history, which of course is not absolutely necessary, and the absence of any palmar and plantar keratosis, cast some doubt on this diagnosis, especially in view of its long duration.

DR. GEORGE M. MACKEE: Dr. Cannon might try vitamin A therapy, using 200,000 to 300,000 U. S. P. units a day, to see what effect that might have on the disease.

DR. FRED WISE: I agree with the clinical diagnosis of Darier's disease.

DR. A. BENSON CANNON: It was suggested that Miss M., whom I showed before this society last month (ARCH. DERMAT. & SYPH. **44**:516 [Sept.] 1941), might have hyperkeratosis follicularis, as described by Drs. Kyrle and Pawloff. On abstracting the article, I could note a striking resemblance of the lesions described to those of Miss M., and I think it is not unlikely that that is the diagnosis of her case.

DR. HOWARD FOX: I agree with the diagnosis in this case. Most dermatologists believe that they can make a positive diagnosis of a classic case of Darier's disease. Yet, the patient of whom Dr. Cannon spoke was presented by me for the first time before this society (ARCH. DERMAT. & SYPH. **19**:515 [March] 1929), and every member present agreed with the diagnosis of Darier's disease. Recently when Dr. Cannon presented the patient again, no one thought the condition was Darier's disease.

DR. A. BENSON CANNON: The patient presented tonight is altogether unlike Mrs. M. in that this man's lesions are most characteristic of Darier's disease and occupy the classic location for that disease. He also has warty-like lesions of the palms and soles and similar lesions behind the last molars on the left side of the jaw. Furthermore, a histologic examination on two occasions, done at different laboratories, showed the characteristic picture of Darier's disease. I hope to give this patient 200,000 U. S. P. units of vitamin A daily and again present him to show the result.

Arsenical Pigmentation and Keratoses Following Dermatitis Herpetiformis. Presented by DR. EUGENE F. TRAUB.

E. G., a man aged 24, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 10, 1941 with a generalized eruption of four years' duration. The eruption began on the right buttock with blisters which broke, crusted and healed, leaving pigmented spots. Three years ago the patient began taking solution of potassium arsenite U. S. P. in doses of 3 to 10 drops three times a day. About one year later he noticed warty lesions beginning to appear on his hands. He continued to take arsenic at intervals up to the present because he found that to be the only medication which gave him relief from the intense itching.

At present the skin of the entire body is irregularly pigmented with small spotty areas with clear skin between the pigmented spots. There are also many scattered, somewhat grouped excoriated lesions. The skin is dry and in some places shows a fine scaling. There is considerable hyperkeratosis, and numerous warty lesions are seen on the palms and soles. There are a few discrete punctate keratoses on the dorsal aspects of the fingers. Occasionally grouped bullous lesions still occur.

The Wassermann and Kahn reactions of the blood were negative. The urine was normal. Examination of the blood for arsenic gave negative results. Histologic examination of a lesion taken from the dorsum of the hand showed keratoses and of a lesion from the left arm showed an inflammatory reaction.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

Lupus Erythematosus. Carcoidosis? Presented by Dr. A. Benson Cannon.

J. De R., an Italian aged 34, a shipping clerk, was first seen at Vanderbilt Clinic in January 1941, complaining of multiple cutaneous lesions which had begun ten years before following an attack of erysipelas behind the right ear. The erysipelas was severe, with high fever and coma lasting for five days, followed by loss of all the hair and a loss in weight of 19 pounds (8.5 Kg.). One month later the present eruption appeared on the face, arms and trunk, accompanied by swelling and pain on motion of the hands. For sixteen months he received injections said to be for rheumatism three times a week in the arm and in the hip. The condition on the hands did not improve, and the shoulders became involved. He had various types of treatment, including gold sodium thiosulfate, a bismuth compound and autogenous vaccines, without improvement except for lessening of redness in the cutaneous lesions. Four years ago pain developed in the feet similar to that in the hands and shoulders. Today he has discomfort in the hands and feet only when jarred. He can feel objects only when they are firmly grasped.

The patient was born in New York and has always lived here. He is the fifth of twelve children, the first five and the twelfth being still alive, the others having died in infancy of unknown causes. The patient did not walk until he was 6 years old because of "weakness" in the hips.

Examination shows a small, poorly developed, thin man who holds his arms semiflexed and his fingers in a grasping position contracted on the palms. The cutaneous lesions involve the scalp, face and upper portions of the forearms, the lower part of the back and the flanks, with deformity and deep cutaneous changes of the hands and fingers. There are several bald, atrophic areas on the scalp, varying in size from that of a nickel to that of a silver dollar, with one palm-sized lesion. There is diffuse atrophy with erythema and scaling of the cheeks. On the back are palm-sized brownish yellow circinate lesions. The borders are raised, red around the centers and atrophic. There are atrophic and white areas on the shoulders, arms and elbows. The fingers are contracted in a semiflexed position. The skin is tense and hard. There is no atrophy of the muscles. The dorsa of the hands are edematous. Examination shows opacities of the cornea of both eyes. Many teeth are missing. His blood pressure is 110 systolic and 72 diastolic. General physical examination showed no abnormalities except those mentioned. All of the superficial lymph nodes are palpable. The fingers are stubbed, and the nails are either absent or deformed. The sensations of heat, cold and pain are present in the fingers. The phalangeal joints are fixed. The axillary and popliteal nerve trunks are enlarged.

Roentgenograms of the hands showed a bony decalcification involving all the fingers and an obliteration of all the joint spaces distal to the carpals. Cystic degeneration and excavation of the bone adjacent to the articular ends were present with hypertrophic changes and partial subluxation. The changes were fairly typical of advanced rheumatoid arthritis with resultant deformity. There was a similar condition present in the bones of the feet. Roentgenograms of the lungs showed discrete puerile tuberculous foci at the hilus and in the central fields of the right lung. A test with old tuberculin in a dilution of 1 to 10,000 elicited a positive reaction, with an inflamed area measuring about 8 cm. in diameter. The urine was normal. The Wassermann reaction of the blood was negative. A blood count showed 6,650,000 erythrocytes and 15,700 leukocytes, with a differential count of 72 per cent polymorphonuclear leukocytes, 19 per cent small and 8 per cent large lymphocytes and 1 per cent eosinophils; there was 16 Gm. of hemoglobin per hundred cubic centimeters. Histologic examination of a specimen taken from the face was reported as lupus erythematosus.

DISCUSSION

Dr. George M. MacKee: I agree with the diagnosis of lupus erythematosus and sarcoidosis in combination.

Dr. J. Gardner Hopkins: As I understand it, there is no histologic evidence of sarcoid and the high reactivity to tuberculin would make one hesitate to make

the diagnosis of sarcoid even in the presence of suggestive histologic changes. The roentgenologist's interpretation of the lesions of the bones of the hand was that an atrophic arthritis was present.

DR. EUGENE F. TRAUB: While in Boston I learned about a new test, known as the Nickerson test, which is an apparently specific test for sarcoid. It is an intradermal test, and it might be well to try it in this case and see if a positive result is obtained.

DR. A. BENSON CANNON: I am by no means certain of the diagnosis of sarcoidosis. I thought the lesions on this patient's trunk were characteristic of sarcoid, while the ones on the face and scalp were typical of lupus erythematosus. Furthermore, the roentgenographic findings in the bones of the feet and hands, notably the decalcification and the cystic formation, were much more suggestive of sarcoidosis than of arthritis.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. FRED WISE.

D. K., a man aged 67, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 14, 1939, with cutaneous lesions of two years' duration. At that time the eruption consisted of yellowish brown mottled areas scattered over the chest, abdomen and thighs and discoid, nummular, infiltrated plaques on the thighs and legs. The clinical diagnosis was "dermatitis." The histologic diagnosis of a lesion of the right thigh was "superficial dermatitis, not characteristic of any clinical entity." The patient was treated with antipruritic emollient lotions and weekly generalized exposures with a quartz mercury vapor glow lamp. On Dec. 10, 1940 ammoniated mercury and salicylic acid salve was prescribed for "a severe acne varioliformis of the scalp."

The patient was brought to my attention on Feb. 18, 1941 because of the spread of the eruption, the complaint of more severe itching and the evolution of the cutaneous lesions manifesting a clinical picture resembling mycosis fungoides.

Two years ago red blotches appeared on the inner surfaces of the thighs and legs. A year ago the upper extremities, four months ago the scalp and lately the sides of the neck, the shoulders and the front of the chest have become successively affected. For the past two weeks blisters have developed in the last-mentioned areas. These blisters burst by themselves or on slight irritation. The fluid was "brownish, sticking like mucilage." The patches make their appearance first as red spots or blotches "like a solution spread out on the skin." Some lesions seem to vanish after varying periods, while new ones appear in the adjacent areas. Others are persistent, rise above the surface of the skin and later become rough and flaky.

The lesions today are generalized, except for the palms and soles, multiform and symmetric. They consist of vesicles and ruptured bullae, plaques and superficial patches, the intervening areas being normal. All surfaces are involved, with greater predilection for the flexor surfaces. The entire scalp is studded, more profusely at the vertex, with pea-sized to almond-sized, hemorrhagic, raw or crusted areas, the remains of ruptured bullae. Located within the patches of the left mammary region are a few firm, tense vesicles with clear fluid contents. The patches vary from well marginated pea-sized to palm-sized, discrete and confluent, nonscaly, smooth and erythematous patches to the solid dull red, rough, padlike indurated plaques covered with adherent furfuraceous scaling and to large superficial, less clearly defined, crescentic and irregular areas spread over the entire back. The nummular plaques are not modified by diascopic pressure. The older lesions are located on the back, thighs and legs. On the back are numerous seborrheic keratoses. There are no palpably enlarged nodes. The buccal mucosa is studded with papules of Fordyce's disease.

The routine laboratory tests gave normal results except for the chemical examination of the blood, which showed 23.5 mg. of urea nitrogen and 5.2 mg. of uric acid per hundred cubic centimeters.

Histologic examination of a specimen taken from a lesion in the right scapular region was made by Dr. Satenstein and Dr. Sachs and "suggests the microscopic picture of mycosis fungoides, with the following description: In the upper and middle parts of the cutis the vessels are dilated and there is in part a diffuse cellular infiltration. There is a moderate interstitial edema throughout the cutis, especially in the papillary bodies. The epidermis is irregularly acanthotic, and in some areas there is a moderate interstitial edema. In several areas there are small vesicles within the epidermis, and about them there is little or no edema. These cavities contain a moderate number of cellular elements similar to those found in the cellular infiltrate below. The cellular infiltrate is composed of small round cells, wandering connective tissue cells and a good number of histiocytes. There are occasional mitotic figures present. There is also a reticulum present in some areas. The reticulum, the polymorphic cellular infiltration, the mitosis and Pautrier's abscesses are all in favor of a diagnosis of mycosis fungoides."

DISCUSSION

Dr. George M. MacKee: While the histologic picture may be suggestive of mycosis fungoides, I do not think it is sufficiently characteristic for that diagnosis. I have never seen or heard of mycosis fungoides being associated with bullous lesions. It is possible, of course, to have a bullous dermatitis medicamentosa engrafted on mycosis fungoides, but it seems unnecessary to go that far to explain the bullae in this case. I thought of the possibility of a Senear-Usher syndrome, but after I looked at the patient from a distance, the dark oval lesions scattered over the body, eczematized but not infiltrated as in mycosis fungoides, suggest a phenolphthalein eruption. One must bear in mind that the eruption might have been modified by roentgen ray treatment. However, a drug eruption should be considered, because oval eczematoid lesions and bullous lesions are occasionally caused by phenolphthalein. This patient even has a bullous lesion in the mouth and bullous lesions on the scalp, and some of the oval plaques on the body are capped with bullous lesions.

Dr. Howard Fox: From the clinical standpoint, I do not think this condition is mycosis fungoides. It is rare to see such a generalized, profuse and symmetric eruption in this disease. Furthermore, there were no lesions in the form of circles or semicircles, and infiltration of the patches was uniform. The presence of bullae on the skin and in the mouth certainly speaks against mycosis fungoides. I think pemphigus should be considered, as the patient is a middle-aged Jew who emigrated from Russia and as the disease is accompanied by lesions in the mouth. Against a drug eruption is the statement of the patient that he has not taken any drugs by mouth or received any kind of injections.

Dr. J. Frank Fraser: The histologic picture does not in the slightest degree resemble that of mycosis fungoides. A phenolphthalein eruption may resemble in its gross appearance the lesions of mycosis fungoides. In my opinion this case is not one of mycosis fungoides.

Dr. Jerome Kingsbury: I think the diagnosis of mycosis fungoides can well be questioned. I do not think the lesions are those ordinarily seen in cases of mycosis fungoides. The man has symmetric erythematous plaques and bullae. He is well nourished; in fact, he is overnourished.

Book Reviews

Essentials of Dermatology. By Norman Tobias, M.D. Price, $4.75. Pp. 478, with 115 illustrations and 12 tables. Philadelphia: J. B. Lippincott Company, 1941.

The author presents a small book on dermatology that should be well received by the general practitioner, by the medical student and by the beginner in dermatology. The book is well organized, and the subject matter is presented in a clear and concise manner. Despite its small size, the book contains descriptions or brief mention of all common, uncommon and even rare dermatologic conditions. The illustrations are numerous. Several charts for differential diagnosis of common dermatoses will be found helpful in making diagnoses. The common dermatoses are discussed from the clinical, etiologic and therapeutic standpoints. The histologic changes are not given for many dermatoses, while for others the descriptions are brief and inadequate.

The subject of therapy has been well presented and includes general medical measures, as well as the common physical and chemical agents employed in dermatologic therapy. The most recent concepts and therapeutic measures are mentioned. The author has compiled a list of general therapeutic suggestions on what to do and what not to do in the management of cutaneous diseases. These measures should be kept in mind by all who treat dermatologic conditions.

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